1 UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY
2
3 CIVIL ACTION NO.
83-2864-SA
ANTONIO CIPALLONE, INDIVIDUALLY
4 AND AS EXECUTOR OF THE ESTATE
OF ROSE D. CIPALLONE,
5
PLAINTIFF, ORAL DEPOSITION OF
6
VS. JEROME M. FELDMAN,
7 M.D.
LIGGETT GROUP, INC., A
8 DELAWARE CORPORATION,
PHILIP MORRIS, INC., A
9 VIRGINIA CORPORATION, AND
LOEWS THEATERS, INC., A
10 NEW YORK CORPORATION,
11 DEFENDANTS.
12
13 * * * * *
FRIDAY, AUGUST 21, 1987
14 * * * * *
15
TRANSCRIPT IN THE ABOVE MATTER TAKEN
16 AT THE OFFICES OF BROWN & CONNERY, ESQUIRES, 300
HADDON AVENUE, WESTMONT, NEW JERSEY, COMMENCING AT
17 9:30 A.M.
18
A P P E A R A N C E S:
19
20 BUDD, LARNER, KENT, GROSS, PICILLO,
ROSENBAUM, GREENBERG & SADE, ESQUIRES
21 BY: CYNTHIA A. WALTERS, ESQUIRE
ATTORNEYS FOR THE PLAINTIFF
22
23 WEBSTER & SHEFFIELD, ESQUIRES
BY: FRANCIS K. DECKER, JR., ESQUIRE
24 -AND-
ROBERT OGDEN COHEN, ESQUIRE
25 ATTORNEYS FOR THE DEFENDANT/LIGGETT GROUP

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1 A P P E A R A N C E S:

2

SHOOK, HARDY & BACON, ESQUIRES
3 BY: PATRICK M. SIRRIDGE, ESQUIRE
-AND-
4 ROBERT NORTHRIP, ESQUIRE
-AND-
5 DONALD KEMNA, ESQUIRE
ATTORNEYS FOR THE DEFENDANTS/PHILIP MORRIS,
6 INC. AND LORILLARD, INC.

7

BROWN & CONNERY, ESQUIRES
8 BY: MICHAEL J. VASSALOTTI, ESQUIRE
ATTORNEYS FOR THE DEFENDANT/PHILIP MORRIS,
9 INC.

10

STRYKER, TAMS & DILL, ESQUIRES
11 BY: JEANNE SZAFRANOWSKI, ESQUIRE
ATTORNEYS FOR THE DEFENDANT/LORILLARD, INC.
12

13 A L S O P R E S E N T:

14 JANE ASCHEMAN, ANALYST

15

16

17 CERTIFIED SHORTHAND REPORTING SERVICES
ARRANGED THROUGH
18 MASTROIANNI & FORMAROLI, INC.
SUITE 310
19 2201 ROUTE 38
CHERRY HILL, NEW JERSEY 08002
20 (609) 964-3440

21

22

23

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1 W I T N E S S I N D E X

2 EXAMINATION OF DR. FELDMAN BY MS. WALTERS:
PAGE 4
3

4 E X H I B I T S

5 EXHIBITS P-FELDMAN-1A THROUGH P-FELDMAN-1X
6 PAGE 86

7 EXHIBIT P-FELDMAN-2
PAGE 87
8

EXHIBIT P-FELDMAN-3
9 PAGE 101

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]feldman (REQUEST)
136,25 157,15 231,19

(OBJECTION)

10,23	15,13	16,19	17, 3	19,20
20, 9	23,14	26,12	26,20	29, 2
31,21	34,17	48,10	53,15	56,11
57,22	60,24	60,25	65,19	66, 2
73,11	74,23	78,11	79, 5	79,13
80, 8	80,21	84,18	92,25	96,20
97, 3	97,20	114,13	117,22	120, 5
125,12	126,24	132, 8	134, 2	141,20
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224,13	225,19	225,25	227, 3	

(DIRECTION)

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1 (IT IS AGREED BY AND BETWEEN
2 COUNSEL THAT ALL OBJECTIONS, EXCEPT AS TO
3 THE FORM OF THE QUESTION, BE RESERVED
4 UNTIL THE TIME OF TRIAL.)
5 (JEROME M. FELDMAN, M.D., HAVING BEEN DULY SWORN,
6 WAS EXAMINED AND TESTIFIED AS FOLLOWS:)
7 (EXAMINATION OF DR. FELDMAN BY MS. WALTERS:)
8 Q. DR. FELDMAN, MY NAME IS CYNTHIA WALTERS. WE
9 MET OFF THE RECORD. I REPRESENT THE PLAINTIFF IN
10 THIS CASE.
11 HAVE YOU EVER BEEN DEPOSED BEFORE?
12 A. YES.
13 Q. HOW MANY TIMES?
14 A. ONE TIME.
15 Q. ARE YOU FAMILIAR WITH DEPOSITION PROCEDURES
16 THEN?
17 A. WELL, I'M ROUGHLY FAMILIAR WITH THEM.
18 Q. LET ME JUST REVIEW THEM WITH YOU. THIS IS A
19 PROCEEDING UNDER OATH. EVERYTHING THAT YOU ARE
20 SAYING TODAY, ALL MY QUESTIONS AND ALL YOUR
21 RESPONSES ARE BEING TAKEN DOWN BY THE SHORTHAND
22 REPORTER SITTING TO MY LEFT. IT WILL BE TYPED UP
23 IN A BOOK AND IT WILL BE AVAILABLE FOR USE, FUTURE
24 USE IN THIS CASE. BECAUSE YOU ARE UNDER OATH, YOU
25 ARE BOUND BY YOUR ANSWERS. IF I ASK A QUESTION

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1 THAT YOU DO NOT UNDERSTAND, PLEASE LET ME KNOW
2 THAT YOU DO NOT UNDERSTAND IT. IF YOU DO ANSWER A
3 QUESTION, WE WILL ASSUME THAT YOU HAVE UNDERSTOOD
4 IT. IS THAT CLEAR?
5 A. YES, IT IS.
6 Q. IF YOU NEED A BREAK AT ANY TIME, LET ME
7 KNOW.
8 MR. SIRRIDGE: CAN I ADD SOMETHING
9 FOR THE RECORD AT THIS POINT? THERE'S BEEN SOME
10 CONFUSION BEFORE, BUT I WANT THE RECORD TO REFLECT
11 THAT REVIEW AND SIGNATURE ARE NOT WAIVED.
12 BY MS. WALTERS:
13 Q. IT'S IMPORTANT THAT YOU ANSWER QUESTIONS
14 VERBALLY BECAUSE THE REPORTER CANNOT TAKE DOWN A
15 NOD OF THE HEAD OR A GESTURE.
16 A. YES.
17 Q. DOCTOR, PURSUANT TO THE SIRRIDGE/NORTHRIP
18 RULE, I HAVE YOUR CHECK FOR TODAY'S DEPOSITION IN
19 THE AMOUNT OF TWO THOUSAND DOLLARS (HANDING).
20 A. THANK YOU VERY MUCH.
21 Q. YOU'RE WELCOME.
22 DOCTOR, YOU SAID YOUR DEPOSITION HAS BEEN
23 TAKEN ON ONE OTHER OCCASION. WHEN WAS THAT?
24 A. IT WAS ROUGHLY ABOUT SIX OR SEVEN YEARS
25 AGO. I CAN'T REMEMBER THE PRECISE DATE BUT IT WAS

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1 SIX OR SEVEN YEARS AGO.

2 Q. WERE YOU AN EXPERT OR A PARTY IN THE CASE?

3 A. I WAS AN EXPERT.

4 Q. WHAT TYPE OF CASE WAS THAT?

5 A. IT WAS A MEDICAL MALPRACTICE CASE.

6 Q. AND WHAT WAS THE MEDICAL ISSUE THAT YOU WERE

7 TESTIFYING ABOUT?

8 A. I WAS TESTIFYING ON BEHALF OF THE PLAINTIFF

9 ABOUT THE QUALITY OF MEDICAL CARE THAT A PATIENT

10 RECEIVED THAT HAD DIABETES AND DIABETES

11 KETOACIDOSIS.

12 Q. HAVE YOU EVER BEEN RETAINED AS AN EXPERT IN

13 ANY OTHER CASE?

14 A. NO, I HAVE NOT.

15 Q. HAVE YOU EVER CONSULTED WITH ANY ATTORNEYS

16 ON ANY OTHER CASE OTHER THAN THIS ONE AND THE ONE

17 THAT YOU JUST DISCUSSED, THE MALPRACTICE CASE?

18 A. MY RECOLLECTION, THIS WAS A LONG TIME AGO,

19 WAS THAT THE ATTORNEY FOR THE CASE WHERE I ACTED

20 AS A WITNESS SENT ME ANOTHER CASE AND I JUST

21 BRIEFLY REVIEWED IT BY MAIL, BUT I'VE FORGOTTEN

22 THE NATURE, BUT I CHOSE NOT TO BE INVOLVED AS AN

23 EXPERT WITNESS IN IT. SO IT WAS KIND OF A

24 ONE-HOUR DEAL BY MAIL REVIEWING IT, AND I DON'T

25 REMEMBER THE NATURE OF IT, IN FACT.

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1 Q. DOCTOR, WHAT IS YOUR PRESENT POSITION?

2 A. MY PRESENT POSITION IS ASSOCIATE PROFESSOR

3 OF MEDICINE AT DUKE UNIVERSITY MEDICAL CENTER IN

4 DURHAM, NORTH CAROLINA.

5 Q. HOW LONG HAVE YOU HELD THAT POSITION?

6 A. I HAVE HELD THAT POSITION -- I'VE HELD THE

7 POSITION AT DUKE UNIVERSITY FOR 19 YEARS. IN THE

8 EARLIER YEARS, IT WAS AT A POSITION AS, YOU KNOW,

9 AN ASSOCIATE IN MEDICINE ASSISTANT PROFESSOR AND

10 THEN LATER AS ASSOCIATE PROFESSOR.

11 Q. SO YOU'VE BEEN A PROFESSOR OF ONE RANK OR

12 ANOTHER AT DUKE UNIVERSITY MEDICAL CENTER FOR THE

13 PAST 19 YEARS?

14 A. THAT IS CORRECT.

15 Q. WHAT DOES YOUR WORK INVOLVE?

16 A. MY WORK INVOLVES A COMBINATION OF PATIENT

17 CARE, RESEARCH AND TEACHING OF THE MEDICAL

18 STUDENTS, HOUSE STAFF AND OTHER PARAMEDICAL

19 PERSONNEL AT THE MEDICAL CENTER.

20 Q. WHAT PERCENTAGE OF YOUR TIME IS INVOLVED IN

21 PATIENT CARE?

22 A. WELL, IT'S PROBABLY EASIER TO GIVE IT IN

23 HOURS. I TEND TO WORK A 80-HOUR WEEK SO I WOULD

24 SAY THAT PROBABLY -- LET ME GIVE IT IN

25 PERCENTAGES. ABOUT 25 PERCENT WOULD BE PATIENT

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1 CARE, 25 TO 35 PERCENT. PROBABLY AN EQUAL AMOUNT
2 WOULD BE RESEARCH AND MAYBE RESEARCH WOULD BE MORE
3 LIKE 50 PERCENT, BUT THE RESEARCH AND THE PATIENT
4 CARE OVERLAP QUITE CONSIDERABLY BECAUSE MY
5 RESEARCH IS IN AREAS OF CLINICAL RESEARCH DEALING
6 WITH IMPROVED CARE FOR PATIENTS. AND, FINALLY,
7 THE TEACHING PORTION IS ABOUT 25 PERCENT. SO I
8 WOULD SAY ROUGHLY IT'S 25/50/25 WITH A BIG OVERLAP
9 BETWEEN THE RESEARCH AND THE PATIENT CARE OF THAT
10 25.
11 Q. HAS THIS PERCENTAGE HELD TRUE FOR THE PAST
12 19 YEARS?
13 A. YES, IT HAS HELD TRUE IN GENERAL.
14 Q. HAVE YOU HAD ANY OTHER POSITIONS DURING THE
15 PAST 19 YEARS OUTSIDE OF DUKE UNIVERSITY MEDICAL
16 CENTER?
17 A. WELL, I AM, IN ADDITION TO BEING IN DUKE
18 UNIVERSITY CENTER, DUKE UNIVERSITY MEDICAL CENTER
19 HOSPITAL, I'M ALSO AT THE DURHAM V.A. MEDICAL
20 CENTER HOSPITAL WHICH IS PART OF THE MEDICAL
21 CENTER COMPLEX AND I'M THE CHIEF OF ENDOCRINOLOGY
22 AND METABOLISM THERE.
23 MR. SIRRIDGE: THAT'S VETERANS
24 ADMINISTRATION.
25 THE WITNESS: VETERANS ADMINISTRATION

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1 HOSPITAL.

2 BY MS. WALTERS:

3 Q. IS THAT HOSPITAL A PART OF THE SAME COMPLEX

4 THAT DUKE UNIVERSITY MEDICAL CENTER IS?

5 A. YES, IT'S CONSIDERED PART OF THE DUKE

6 UNIVERSITY MEDICAL CENTER WITH THE UNIVERSITY

7 BEING ONE PART AND THE VETERANS ADMINISTRATION

8 BEING ANOTHER ARM OF THE SAME MEDICAL CENTER.

9 Q. ARE THEY IN THE SAME BUILDING?

10 A. NO. THEY'RE ON THE SAME CAMPUS. THEY'RE

11 SEPARATE BUILDINGS. DUKE IS MADE OF A NUMBER OF

12 DIFFERENT BUILDINGS.

13 Q. THE PERCENTAGES YOU'VE GIVEN ME IN TERMS OF

14 PATIENT CARE, RESEARCH, TEACHING, ALSO APPLY TO

15 DURHAM OR ALSO INCLUDE THE WORK AT DURHAM V.A.

16 MEDICAL CENTER?

17 A. YES, THAT WOULD BE THE OVERALL PROPORTION

18 BETWEEN THE TWO PLACES, THE APPROXIMATE OVERALL

19 PROPORTION.

20 Q. AND YOU DO PATIENT CARE AT BOTH

21 INSTITUTIONS?

22 A. YES, I DO.

23 Q. AND YOU DO RESEARCH AT BOTH INSTITUTIONS?

24 A. YES.

25 Q. AND YOU DO TEACHING AT BOTH INSTITUTIONS?

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1 A. AT BOTH INSTITUTIONS. I DON'T KNOW IF THIS
2 IS RELEVANT. IN ADDITION, I'VE BEEN AN EDITOR OF
3 A MEDICAL JOURNAL, WHICH IS OUTSIDE OF DUKE, FOR
4 THE LAST FOUR-AND-A-HALF YEARS. I DON'T KNOW IF
5 THAT WOULD BE RELEVANT INFORMATION.
6 Q. WHAT IS THAT JOURNAL?
7 A. THAT WOULD BE THE JOURNAL OF CLINICAL
8 ENDOCRINOLOGY AND METABOLISM. I'M ONE OF THE
9 ASSOCIATE EDITORS WITH THE EDITORIAL OFFICE BEING
10 IN CHAPEL HILL, NORTH CAROLINA AT THE UNIVERSITY
11 OF NORTH CAROLINA.
12 Q. AND WHAT PERCENTAGE OF YOUR TIME IS DEVOTED
13 TO THE DUTIES INVOLVED IN THAT EDITORSHIP?
14 A. THAT I DO IN THE EVENING, EVENING AND
15 WEEKENDS. AND I PROBABLY DEVOTE ABOUT FIVE TO
16 EIGHT HOURS A WEEK IN THE EVENINGS OR ON SATURDAY
17 OR SUNDAY. IT'S DISTINCT FROM MY DUTIES AT THE
18 MEDICAL CENTER.
19 Q. DOCTOR, IS YOUR PATIENT CARE WORK EQUALLY
20 DIVIDED BETWEEN DUKE AND DURHAM OR IS THERE A
21 DIFFERENCE?
22 A. WELL --
23 (OBJECTION) MR. SIRRIDGE: OBJECTION. FORM.
24 DUKE AND THE V.A.?
25 MS. WALTERS: WHAT DID I SAY?

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1 MR. SIRRIDGE: YOU SAID DUKE AND
2 DURHAM.
3 BY MS. WALTERS:
4 Q. DUKE AND THE DURHAM V.A. MEDICAL CENTER.
5 A. IT'S APPROXIMATELY EQUALLY DIVIDED ALTHOUGH
6 THE TYPE OF WORK THAT I DO AT THE TWO PLACES IS
7 SOMEWHAT DIFFERENT.
8 Q. HOW DO THEY DIFFER, HOW DOES IT DIFFER?
9 A. WELL, AT THE DURHAM V.A., I'M THE CHIEF OF
10 ENDOCRINOLOGY AND METABOLISM SO PATIENT CARE AND
11 SOME OF MY RESEARCH INVOLVES A SUBSTANTIAL AMOUNT
12 OF TIME ON DIABETES BECAUSE I SEE ALL THE PATIENTS
13 WITH DIABETES AT THE DURHAM VETERANS
14 ADMINISTRATION HOSPITAL.
15 Q. DO YOU SEE -- I'M SORRY. GO AHEAD.
16 A. IN ADDITION, I'LL SEE THE PATIENTS AT THE
17 DURHAM VETERANS ADMINISTRATION HOSPITAL, ALL THE
18 PATIENTS THAT I'M CALLED TO SEE THAT HAVE
19 ENDOCRINE-TYPE TUMORS. NOW, AT DUKE UNIVERSITY,
20 MY CLINICAL DUTIES ARE MAINLY WITH THE PATIENTS
21 THAT HAVE ENDOCRINE-TYPE TUMORS AND I REALLY DON'T
22 DIRECTLY SEE PATIENTS WITH DIABETES. SO IT'S ALL
23 SORT OF TUMORS AT DUKE AND A MIXTURE AT THE V.A.
24 Q. WHERE DID THE PATIENTS COME FROM? ARE THESE
25 PATIENTS THAT COME TO YOU DIRECTLY OR ARE THEY

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1 PATIENTS THAT YOU SEE ON A CONSULTATION BASIS?
2 A. THE MAJORITY WOULD BE PATIENTS THAT I --
3 WELL, THERE'S TWO GROUPS OF PATIENTS THERE. AT
4 THE VETERANS ADMINISTRATION HOSPITAL, I'LL SEE
5 VETERANS THAT COME TO THE MEDICAL CENTER EITHER BY
6 REFERRAL BY ANOTHER V.A. HOSPITAL OR SELF-REFERRED
7 FOR CARE. THEY MAY NOT COME SPECIFICALLY TO ME
8 BUT THEY COME BECAUSE OF A PROBLEM WITH
9 ENDOCRINOLOGY METABOLISM OR IN SOME CASES
10 ENDOCRINE TUMORS.
11 Q. AND YOU BECAME THEIR PRIMARY TREATING
12 DOCTOR?
13 A. I BECAME THEIR PRIMARY TREATING DOCTOR
14 WORKING WITH THE RESIDENTS AND THE INTERNS AT THE
15 MEDICAL CENTER.
16 Q. AND THAT'S THE MAJORITY OF THE DURHAM V.A.
17 MEDICAL CENTER PATIENTS THAT YOU SEE?
18 A. THAT'S RIGHT, RIGHT. THAT'S CORRECT.
19 Q. AND WHAT ABOUT WITH RESPECT TO THE DUKE
20 UNIVERSITY MEDICAL CENTER?
21 A. DUKE UNIVERSITY MEDICAL CENTER, MY PRACTICE
22 IS MORE BY CHOICE MORE RESTRICTED AND SO THAT'S
23 PATIENTS WITH ENDOCRINE TUMORS SUCH AS CARCINOID
24 TUMORS AND PHEOCHROMOCYTOMA TUMORS, SOMETIMES
25 ABBREVIATED PHEOS, P-H-E-O-S.

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1 Q. YOU SAY YOUR PRACTICE IS LIMITED BY CHOICE
2 TO THOSE PATIENTS?
3 A. YES.
4 Q. WHY IS THAT?
5 A. WELL, BECAUSE I'M SO BUSY WITH ALL MY
6 ACTIVITIES, AND AT THE DUKE UNIVERSITY, WE HAVE A
7 NUMBER OF DOCTORS WHO ARE EXTREMELY CONFIDENT IN
8 DIABETES THAT CAN SEE THE PATIENTS WITH DIABETES
9 THAT ARE PRIMARILY INTERESTED IN A PRIVATE
10 PRACTICE SITUATION. SO I FEEL LIKE THAT THE
11 PATIENTS WITH DIABETES CAN GET VERY GOOD CARE
12 WITHOUT MY PARTICIPATION WHEREAS WITH THE
13 ENDOCRINE PATIENTS, I HAVE SORT OF UNIQUE
14 EXPERIENCE SO I SEE THOSE PATIENTS --
15 Q. ARE THOSE PRIMARILY CONSULTATION OR DO YOU
16 BECOME THE DIRECT PRIMARY TREATING DOCTOR IN THOSE
17 CASES?
18 A. THEY ARE PRIMARILY CONSULTATION.
19 Q. AND WHO REFERS THEM TO YOU?
20 A. THEY'RE REFERRED BY A MAJORITY OF THE
21 SPECIALISTS AND SUBSPECIALISTS AT THE MEDICAL
22 CENTER. FOR INSTANCE, THE MAJOR SOURCES OF THE
23 REFERRALS WOULD BE THE ONCOLOGISTS,
24 GASTROENTEROLOGISTS, THE GENERAL SURGEONS,
25 THORACIC SURGEONS AND THEN ALMOST ALL THE OTHER

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1 SPECIALTIES FROM TIME TO TIME WILL REFER A
2 PATIENT, PEDIATRICS OCCASIONALLY, NEUROLOGY AND SO
3 FORTH. OCCASIONALLY, PATIENTS ARE REFERRED FROM
4 THEIR PHYSICIAN OUTSIDE OF DUKE AND I'LL SEE THEM
5 IN CONSULTATION. USUALLY --
6 Q. HOW OFTEN DOES THAT HAPPEN?
7 A. THAT HAPPENS RECENTLY PROBABLY A PATIENT
8 EVERY COUPLE OF WEEKS. IT'S NOT A LARGE NUMBER AT
9 ALL. IN GENERAL, WHAT I'VE TRIED TO DO WHEN I GET
10 CALLS IS TO GET THE PATIENTS TO SEE ONE OF THE
11 ONCOLOGISTS, SOMEONE AS A PRIMARY PHYSICIAN, AND
12 THEN I ACT AS A CONSULTANT IN THAT CASE BECAUSE,
13 AGAIN, BECAUSE OF MY TIME CONSTRAINTS, I DON'T
14 HAVE MUCH TIME TO SEE THEM.
15 Q. HOW MANY PATIENTS WOULD YOU SEE IN A YEAR
16 FROM THE DUKE UNIVERSITY MEDICAL CENTER THAT HAVE
17 ENDOCRINE TUMORS?
18 A. WELL, IN RECENT YEARS, IT'S CHANGED OVER THE
19 YEARS AND THE NUMBER HAS TENDED TO INCREASE. SO
20 WHAT I'M TALKING ABOUT NOW, LET'S SAY, WOULD BE A
21 REPRESENTATIVE OF THE LAST THREE YEARS, THE LAST
22 THREE COMPLETE YEARS, '86, '85, '84. AND I WOULD
23 END UP SEEING APPROXIMATELY 35 TO 40 PATIENTS WITH
24 CARCINOID TUMORS IN A YEAR. I WOULD SEE
25 APPROXIMATELY FIVE PATIENTS THAT TURN OUT TO HAVE

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1 PHEOCHROMOCYTOMAS IN A YEAR. I WOULD SEE TWO OR
2 THREE PATIENTS THAT HAVE ADRENAL CORTICAL TUMORS
3 IN A YEAR. AND THEN I WOULD SEE ADDITIONALLY AT
4 LEAST AN EQUAL NUMBER OF PATIENTS OR EVEN MORE WHO
5 ARE SUSPECTED OF HAVING THESE THINGS BUT, IN FACT,
6 TURN OUT NOT TO HAVE THESE CONDITIONS, SO THAT'S
7 PEOPLE THAT MIGHT HAVE FLUSHING, UNEXPLAINED
8 DIARRHEA, HYPERTENSION WITH SPELLS AND TURN OUT
9 NOT TO HAVE THE CAUSE BEING AN ENDOCRINE TUMOR.
10 Q. WHAT ARE THE MAJORITY OF THE OTHER CAUSES
11 THAT YOU FIND IN THOSE CASES?
12 A. FOR --
13 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM OF
14 THE QUESTION.
15 BY MS. WALTERS:
16 Q. THE ONES THAT WERE SUSPECTED OF HAVING
17 CARCINOID TUMOR BUT YOU FIND THAT THERE WERE OTHER
18 CAUSES FOR THEIR SYMPTOMS.
19 A. IN SOME CASES, THEY'VE BEEN PEOPLE THAT HAVE
20 MENOPAUSAL SYMPTOMS, MENOPAUSAL HOT FLASHES,
21 PREDOMINANTLY IN MEN, OCCASIONALLY IN WOMEN. MANY
22 OF THEM ARE PATIENTS WHERE THEY'LL HAVE
23 IDIOPATHIC, IN OTHER WORDS, THEY'LL HAVE FLUSHING
24 WHICH IS NOT TOTALLY EXPLAINED. AND THEN, THERE'S
25 ANOTHER GROUP THAT MIGHT HAVE FLUSHING RELATED TO

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1 SOME MEDICATION THEY'RE TAKING, FOR INSTANCE,
2 NITROGLYCERIN OR CALCIUM CHANNEL BLOCKER DRUGS.
3 Q. WHEN YOU SAID YOU HAVE -- I'M SORRY. WERE
4 YOU FINISHED YOUR RESPONSE?
5 A. YES.
6 Q. THOSE ARE THE --
7 A. THAT'S WITH RESPECT TO FLUSHING.
8 Q. YOU HAD MENTIONED OTHER SYMPTOMS, FLUSHING,
9 DIARRHEA, HYPERTENSION AS BEING THE REASON
10 CLINICALLY THAT THESE PATIENTS ARE REFERRED TO
11 YOU; IS THAT CORRECT?
12 A. YES.
13 Q. AND IN THE MAJORITY OF THOSE CASES THAT ARE
14 SUSPECTED BUT WHICH YOU REJECT, YOU FIND OTHER
15 REASONS AND YOU MENTIONED SEVERAL REASONS AND THEN
16 YOU STATED THAT WOULD COVER THE FLUSHING. ARE
17 THERE OTHER REASONS TO COVER THE REST OF THE
18 AREAS?
19 (OBJECTION) MR. SIRRIDGE: I'M GOING TO OBJECT TO
20 THE FORM OF THE QUESTION AS INCORRECTLY
21 SUMMARIZING THE TESTIMONY.
22 BY MS. WALTERS:
23 Q. DID I INCORRECTLY SUMMARIZE THE TESTIMONY,
24 DOCTOR?
25 MR. SIRRIDGE: WHY DON'T YOU READ IT

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1 BACK.

2 (DESIGNATED QUESTION IS READ)

3 (OBJECTION) MR. SIRRIDGE: I STILL OBJECT TO THE

4 FORM.

5 THE WITNESS: ALSO, I SORT OF DON'T

6 LIKE THE WORD "REJECT", THAT I REJECT. I DON'T

7 KNOW WHAT YOU MEAN BY THAT.

8 BY MS. WALTERS:

9 Q. WOULD THE WORD "RULE OUT" BE BETTER, RULE

10 OUT CARCINOID?

11 MR. NORTHRIP: WHY DON'T YOU RESTATE

12 THE QUESTION?

13 MS. WALTERS: OKAY.

14 BY MS. WALTERS:

15 Q. DOCTOR, YOU HAVE APPROXIMATELY, I THINK YOU

16 SAID, AN EQUAL NUMBER OF PATIENTS THAT ARE RULED

17 -- THAT ARE REFERRED TO YOU BECAUSE OF CERTAIN

18 CLINICAL SYMPTOMS?

19 A. THAT'S CORRECT.

20 Q. WHEN YOU SAY "EQUAL NUMBER", ARE YOU TALKING

21 ABOUT APPROXIMATELY 35 TO 40 A YEAR?

22 A. LET'S SEE.

23 MR. SIRRIDGE: ALONG WITH THE

24 ADDITIONAL PATIENTS HE ADDED TO THE 35 AND 40?

25 MS. WALTERS: THAT'S WHAT I'M TRYING

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1 TO FIND OUT.

2 THE WITNESS: I GUESS THAT WOULD BE

3 ANOTHER 45 OR SO.

4 BY MS. WALTERS:

5 Q. AND THIS IS ON AN ANNUAL BASIS?

6 A. THIS WOULD BE ON AN ANNUAL BASIS. THIS IS

7 MY ESTIMATE, ANNUAL BASIS.

8 Q. AND THESE 45, I USED THE TERM "REJECT". YOU

9 FEEL MORE COMFORTABLE WITH YOU RULE OUT AN

10 ENDOCRINE TUMOR?

11 A. YES, RULE OUT FOR THE TIME BEING AN

12 ENDOCRINE TUMOR. SOMETIMES YOU CAN'T TELL UNTIL

13 YOU HAVE FURTHER FOLLOW-UP IF IT MIGHT ULTIMATELY

14 BE AN ENDOCRINE TUMOR, BUT FOR THE MOMENT, YOU

15 DON'T HAVE ANY COMPELLING EVIDENCE IT'S AN

16 ENDOCRINE TUMOR SO FOR THE MOMENT YOU WOULD RULE

17 OUT DEFINITE EVIDENCE.

18 Q. AND THE CLINICAL REASON THAT THESE PATIENTS

19 ARE SENT TO YOU IS BECAUSE THEY HAVE SYMPTOMS OF

20 FLUSHING AND/OR DIARRHEA AND/OR HYPERTENSION; IS

21 THAT CORRECT?

22 A. THAT'S AMONG THE REASONS THEY WOULD BE SENT

23 TO ME. THERE ARE OTHER REASONS ALSO.

24 Q. WHAT ARE THE OTHER REASONS?

25 A. WELL, ONE OF THE REASONS MIGHT BE THAT THE

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1 ONCOLOGISTS HAVE A PATIENT THAT HAS A TUMOR IN
2 THEIR LIVER AND IT APPEARS TO BE A METASTATIC
3 TUMOR AND THE PATIENT TO THE ONCOLOGISTS SEEMS
4 LIKE THEY ARE HEALTHIER THAN A PATIENT SHOULD BE
5 WITH A TUMOR IN THE LIVER. SO THEY WILL ASK ME TO
6 DO TESTS TO SEE IF THE PATIENT MIGHT HAVE A
7 CARCINOID TUMOR. THAT WOULD BE ANOTHER REASON
8 BESIDE FLUSHING OR THE DIARRHEA.
9 SOMETIMES I'M ASKED TO SEE A PATIENT BECAUSE
10 THEY HAVE SURGERY, EXPLORATORY-TYPE SURGERY FOR AN
11 UNKNOWN CONDITION WHERE THE SURGERY SEEMS TO BE
12 INDICATED. AND AT THE TIME OF SURGERY, A
13 CARCINOID TUMOR IS FOUND. IN THAT CASE, THEY WILL
14 ASK ME TO SEE A PATIENT, TO GIVE AN OPINION ABOUT
15 THE THERAPY AND ALSO TO DO APPROPRIATE TESTS OF
16 THE PATIENT. SO THERE ARE OTHER REASONS BESIDE,
17 YOU KNOW, THE PATIENT COMING IN WITH SYMPTOMS.
18 Q. AND IN THAT GROUP OF THE 45, YOU RULE OUT
19 CARCINOID TUMOR BASED ON YOUR TESTS?
20 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM OF
21 THE QUESTION.
22 THE WITNESS: IN THAT GROUP OF 45 --
23 BY MS. WALTERS:
24 Q. I WOULD ASK YOU FOR THE REASONS PEOPLE REFER
25 YOU CASES THAT ARE SUSPECTED OF HAVING CARCINOID

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1 TUMORS WHICH TURN OUT NOT TO BE CARCINOID TUMORS,
2 AND I BELIEVE THAT WAS THE NUMBER 45.
3 A. THAT'S APPROXIMATELY 45.
4 Q. AND THE LAST REASON FOR REFERRAL YOU JUST
5 GAVE WAS AFTER SURGERY THERE WAS A DIAGNOSIS OF
6 CARCINOID TUMOR?
7 MR. SIRRIDGE: HE JUST STATED HE
8 RULED THEM OUT FOR THE TIME BEING.
9 (OBJECTION) MR. NORTHRIP: AND I'M GOING TO
10 OBJECT TO THE FORM BECAUSE I BELIEVE THE ORIGINAL
11 QUESTION YOU ASKED HIM, MISS WALTERS, WHICH I
12 THINK HE WAS CONTINUING TO ANSWER, WAS WHY ARE
13 PATIENTS REFERRED TO YOU. YOU'VE ONLY IN THIS
14 LAST COMMENT ADDED THE QUALIFICATION WHY ARE
15 PATIENTS REFERRED TO YOU THAT YOU SUBSEQUENTLY
16 RULE OUT.
17 MS. WALTERS: NO, ALL THE
18 QUESTIONING, IN THIS LATTER PORTION OF
19 QUESTIONING, HAS DEALT WITH THE 45 PATIENTS THAT
20 ARE REFERRED TO YOU WHICH YOU RULE OUT CARCINOID.
21 MR. SIRRIDGE: FOR THE TIME BEING.
22 MS. WALTERS: FOR THE TIME BEING.
23 BY MS. WALTERS:
24 Q. AND THAT FOURTH REASON THAT YOU GAVE WAS
25 AFTER EXPLORATORY SURGERY, THE CARCINOID TUMOR IS

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1 FOUND AND THEN THEY'RE REFERRED TO YOU FOR THERAPY
2 AND TESTING; IS THAT CORRECT?
3 A. THAT'S RIGHT. THAT'S CORRECT. BUT I WOULD
4 LIKE TO QUALIFY AS FAR AS THE NUMBERS, THAT YOU
5 KNOW, APPROXIMATELY, LET'S SAY, 30 PATIENTS WOULD
6 BE REFERRED BECAUSE OF SYMPTOMS.
7 Q. AND THOSE ARE THE FLUSHING, DIARRHEA AND
8 HYPERTENSION THAT YOU MENTIONED?
9 A. FLUSHING, DIARRHEA AND HYPERTENSION.
10 ANOTHER REASON PEOPLE ARE REFERRED IS ADRENAL
11 MASSES. SO LET'S SAY 30 ARE REFERRED AND ANOTHER
12 APPROXIMATELY 15 COULD COME IN BECAUSE THERE'S
13 SOMETHING LIKE AN ADRENAL MASS WHICH MAY TURN OUT
14 TO BE A PHEOCHROMOCYTOMA. THERE'S A CARCINOID
15 TUMOR DISCOVERED AT SURGERY UNEXPECTEDLY AND SO
16 FORTH.
17 Q. WHAT NUMBER IS THAT WHERE A CARCINOID TUMOR
18 WAS FOUND AT SURGERY THAT LATER TURNS OUT NOT TO
19 BE A CARCINOID?
20 A. NO, THESE ARE ONES THAT TURN OUT TO BE
21 CARCINOID.
22 Q. THAT WASN'T THE QUESTION. ARE THERE ANY?
23 MR. NORTHRIP: I THINK ORIGINALLY IT
24 WAS THE QUESTION.
25 MS. WALTERS: IT WAS NEVER THE

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1 QUESTION. THE DOCTOR MAY HAVE MISUNDERSTOOD IT.
2 BY MS. WALTERS:
3 Q. DOCTOR, ARE THERE ANY OF THE 45 CASES THAT
4 YOU HAVE -- LET'S JUST FINISH AND APPROACH IT A
5 DIFFERENT WAY. OF THE 45 CASES THAT ARE REFERRED
6 TO YOU AS SUSPECTED OF HAVING A CARCINOID IN WHICH
7 YOU LATER RULE OUT, 30 OF THEM YOU SAID ARE
8 REFERRED TO YOU BECAUSE OF THE SYMPTOMS. ANOTHER
9 15 ARE REFERRED TO YOU BECAUSE OF AN ADRENAL MASS
10 THAT TURNS OUT TO BE A PHEOCHROMOCYTOMA?
11 A. THE QUESTIONS ARE SO INVOLVED NOW, I'M SORT
12 OF LOSING TRACK OF WHERE I AM BECAUSE I'M
13 ESTIMATING THESE NUMBERS AND I'M ESTIMATING THAT
14 THERE'S ABOUT AN EQUAL NUMBER OF PATIENTS THAT
15 TURN OUT REFERRED TO ME BECAUSE OF THE FLUSHING,
16 DIARRHEA. THOSE PATIENTS TURN OUT -- SOME OF
17 THOSE TURN OUT NOT TO HAVE A CARCINOID TUMOR,
18 PHEOCHROMOCYTOMA. AND THEN THERE'S APPROXIMATELY,
19 APPROXIMATELY 30 PATIENTS THAT ARE REFERRED
20 BECAUSE OF THE SYMPTOMS THAT WILL TURN OUT TO HAVE
21 THEM. THEN, IN ADDITION, THERE'S 15 OR SO MORE
22 APPROXIMATELY PATIENTS THAT ARE REFERRED FOR
23 SURGICAL FINDINGS, BY SURPRISE THAT THEY HAVE IT,
24 WHO DEFINITELY TURN OUT TO HAVE IT.
25 NOW, THESE ARE JUST ESTIMATES BECAUSE I

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1 WASN'T ASKED TO GO THROUGH MY RECORDS BEFORE I
2 CAME HERE AND TRY AND PRECISELY ESTABLISH THE
3 NUMBER.
4 Q. I UNDERSTAND. I'M JUST TRYING TO GET A
5 CLEARER PICTURE. YOU SAID THAT APPROXIMATELY 30
6 ARE REFERRED TO YOU BECAUSE THEY HAVE SYMPTOMS
7 THAT ARE SUSPECTED OF BEING CARCINOID AND -- LET
8 ME START THAT QUESTION AGAIN.
9 YOU SAID APPROXIMATELY 60 ARE REFERRED TO
10 YOU EACH YEAR BECAUSE THEY HAVE SYMPTOMS THAT ARE
11 SUSPECTED OF BEING CARCINOID. 30 OF THOSE TURN
12 OUT NOT TO BE CARCINOID AND 30 OF THOSE TURN OUT
13 TO BE CARCINOID.
14 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM OF
15 THE QUESTION. IT'S UNDULY CONFUSING.
16 MR. NORTHRIP: I THINK WE MAY HAVE
17 LOST TRACK. I THINK ORIGINALLY, MISS WALTERS,
18 WHEN YOU STARTED ON THIS LINE YOU WERE ASKING
19 ABOUT THE V.A., IS THAT CORRECT, AND I'M NOT SURE
20 NOW WHETHER YOU'RE TALKING ABOUT JUST THE V.A. OR
21 THE ENTIRE PRACTICE.
22 MS. WALTERS: WE'RE TALKING ABOUT
23 DUKE.
24 MR. NORTHRIP: THAT WOULD INCLUDE THE
25 V.A.?

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1 BY MS. WALTERS:

2 Q. I DON'T KNOW. WERE YOU INCLUDING BOTH THE

3 V.A. AND DUKE IN THE NUMBERS YOU HAVE GIVEN ME?

4 A. I'M INCLUDING BOTH THE V.A. AND DUKE AS FAR

5 AS THE TUMOR ASPECTS OF IT IN MY ROLE AS A

6 CONSULTANT ON TUMORS. NOW, I'M NOT INCLUDING THE

7 V.A. AS FAR AS MY ROLE AS A GENERAL INTERNIST

8 SEEING A CERTAIN PERCENTAGE OF PATIENTS AS A

9 GENERAL INTERNIST OR IN MY ROLE SEEING PATIENTS

10 WITH ENDOCRINE DISEASE SUCH AS DIABETES.

11 MS. WALTERS: CAN YOU GO BACK AND

12 READ THE DOCTOR'S TESTIMONY, THE TWO ANSWERS THAT

13 HE GAVE ABOUT THE 30 PATIENTS THAT ARE REFERRED TO

14 HIM.

15 (DESIGNATED QUESTIONS AND ANSWERS ARE

16 READ)

17 BY MS. WALTERS:

18 Q. DOCTOR, I'M GOING TO START OVER AGAIN WITH

19 THE NUMBER 45 THAT YOU GAVE ME AS 45 PATIENTS WHO

20 WERE REFERRED TO YOU AS SUSPECTED OF HAVING

21 CARCINOID AND YOU THEN RULE THAT DIAGNOSIS OUT,

22 CORRECT?

23 MR. SIRRIDGE: AT THAT PARTICULAR

24 TIME.

25 THE WITNESS: AT THAT TIME, YES.

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1 BY MS. WALTERS:

2 Q. AT THAT PARTICULAR TIME, YES.

3 A. OKAY, YES.

4 Q. OF THOSE --

5 MR. NORTHRIP: DID YOU FINISH YOUR

6 ANSWER, DOCTOR?

7 THE WITNESS: SEE, IT'S NOT ONLY

8 THEY'RE SUSPECTED OF CARCINOID, BUT LET'S SAY FIVE

9 OF THEM ARE SUSPECTED OF PHEOCHROMOCYTOMAS, TOO.

10 IN OTHER WORDS, THERE'S A MIXTURE. I'M INTERESTED

11 IN CARCINOIDS, PHEOCHROMOCYTOMAS AND ADRENAL

12 CORTICAL TUMORS. THAT'S THE PREDOMINANT.

13 BY MS. WALTERS:

14 Q. AND 45 ARE REFERRED TO YOU BECAUSE THEY'RE

15 SUSPECTED OF HAVING AN ENDOCRINE TUMOR?

16 A. ENDOCRINE TUMOR IN THE AREAS I'M

17 INTERESTED. SO IF IT WAS 45, IT COULD BE FIVE

18 PHEOS, FIVE ADRENAL CORTICALS AND PERHAPS EVEN

19 WITH THE PHEOS WHEN I RULE IT OUT, I WOULD SAY

20 IT'S MORE LIKE TEN AND FIVE. AND SO THAT LEAVES

21 ABOUT 30 CARCINOIDS APPROXIMATELY.

22 Q. IN THAT GROUP?

23 A. THAT WOULD RULE OUT, 30, RIGHT.

24 Q. AND THOSE 30 ARE ALL REFERRED TO YOU FOR

25 SYMPTOMS OF FLUSHING, DIARRHEA AND HYPERTENSION;

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1 IS THAT CORRECT?

2 A. THAT 30 ARE REFERRED TO ME MAINLY FOR

3 FLUSHING AND DIARRHEA. THE HYPERTENSION IS

4 USUALLY MORE IN THE PEOPLE THAT ARE REFERRED AS

5 POSSIBLE PHEOS, THE TEN PEOPLE, LET'S SAY,

6 REFERRED AS POSSIBLE PHEOS. THAT'S THE

7 HYPERTENSION. SO THAT WOULD BE FLUSHING AND

8 DIARRHEA.

9 Q. DO YOU EVER RULE OUT A CARCINOID TUMOR IN A

10 CASE THAT'S REFERRED TO YOU THAT HAS ALREADY BEEN

11 DIAGNOSED AS HAVING A CARCINOID?

12 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.

13 THE WITNESS: I DON'T --

14 BY MS. WALTERS:

15 Q. YOU CAN ANSWER.

16 A. DO I EVER RULE OUT -- SAY IT ONE MORE TIME.

17 Q. DO YOU EVER RULE OUT A CARCINOID TUMOR IN A

18 CASE THAT HAS ALREADY BEEN HISTOLOGICALLY

19 DIAGNOSED AS HAVING A CARCINOID?

20 (OBJECTION) MR. SIRRIDGE: I STILL OBJECT TO THE

21 FORM, BUT GO AHEAD.

22 THE WITNESS: I WOULD SAY IT WOULD

23 VERY RARELY, WOULD BE EXTREMELY RARE IF IT HAS A

24 HISTOLOGICAL DIAGNOSIS OF CARCINOID THAT I WOULD

25 RULE IT OUT BECAUSE THE TESTS I DO TEND MORE TO

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1 RULE THINGS IN THAN TO RULE THEM OUT AS FAR AS THE
2 TESTS.
3 BY MS. WALTERS:
4 Q. WHY IS THAT?
5 A. WELL, BECAUSE ONE CAN HAVE A CARCINOID
6 TUMOR, WHICH IS IDENTIFIED BY THE PATHOLOGIST WHO
7 SAYS IT IS A TYPICAL OR ATYPICAL CARCINOID TUMOR
8 AND IT MAY NOT PRODUCE THE CHEMICALS THAT I WORK
9 WITH AND, YET, IT IS STILL A CARCINOID TUMOR. SO
10 IF THERE IS STRONG CLINICAL AND PATHOLOGICAL
11 EVIDENCE THAT IT'S A CARCINOID TUMOR, THEN IT
12 WOULD BE UNLIKELY THAT I WOULD RULE IT OUT.
13 Q. OF THE CASES OF CARCINOID THAT -- LET ME
14 JUST ASK YOU -- STRIKE THAT QUESTION.
15 HOW MANY CASES OF CARCINOID DO YOU SEE THAT
16 HAVE ALREADY BEEN DIAGNOSED HISTOLOGICALLY AS
17 HAVING A CARCINOID TUMOR?
18 A. A SUBSTANTIAL NUMBER. I CAN'T GIVE YOU A
19 GOOD ESTIMATE ON THAT, THOUGH.
20 Q. AND WHY --
21 A. BUT IT'S A SUBSTANTIAL NUMBER.
22 Q. DID THE MAJORITY OF YOUR CASES COME TO YOU
23 CARRYING A HISTOLOGIC DIAGNOSIS OF CARCINOID?
24 A. NOT NECESSARILY CARRYING IT, BUT WHERE IT'S
25 SUSPECTED AND THEY WANT ME TO GIVE AN OPINION

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1 ABOUT WHAT I THINK. A GOOD PERCENTAGE WOULD COME
2 WITH THAT REASON FOR BEING REFERRED TO ME.
3 Q. THAT IT'S SUSPECTED?
4 A. IT'S STRONGLY SUSPECTED, AND IN SOME CASES,
5 IT'S HISTOLOGICALLY BEING CONFIRMED, BUT I CAN'T
6 REALLY GIVE YOU -- I'M GETTING INTO PERCENTAGES
7 WHEN I DO THAT THAT ARE BEYOND WHAT I'M REALLY
8 CAPABLE OF ESTIMATING OFF THE TOP OF MY HEAD.
9 Q. SO THE MAJORITY COME TO YOU BECAUSE THEY'RE
10 SUSPECTED OF HAVING CARCINOID TUMORS?
11 A. A GOOD PERCENTAGE DO.
12 Q. AND WHAT'S THE PURPOSE OF THEIR REFERRAL TO
13 YOU?
14 A. TO SEE IF I, INDEED, THINK THEY, IN FACT, DO
15 HAVE CARCINOID TUMORS.
16 Q. BASED ON --
17 A. FREQUENTLY BASED ON MY DOING ADDITIONAL
18 LABORATORY TESTING IN MY SPECIALIZED LABORATORY,
19 RESEARCH LABORATORY, AND, ALSO, BY MY USING MY
20 CLINICAL JUDGMENT AND EXPERIENCE WITH CARCINOIDS
21 TO SEE IF THIS PATIENT, INDEED, IN MY OPINION
22 WOULD HAVE A CARCINOID.
23 Q. NOW, OF THE CASES THAT COME TO YOU ALREADY
24 CARRYING A HISTOLOGIC DIAGNOSIS OF CARCINOID, WHAT
25 IS THE PURPOSE OF THEIR REFERRAL TO YOU?

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1 A. WELL --

2 (OBJECTION) MR. SIRRIDGE: I'M GOING TO OBJECT TO

3 THAT AS BEING ASKED AND ANSWERED, BUT GO AHEAD.

4 THE WITNESS: WELL, AS I DID SAY, IN

5 SOME CASES, I THINK I DID SAY, IN SOME CASES,

6 THEY'RE CARRYING A DIAGNOSIS BUT BECAUSE

7 CARCINOIDS ARE CONSIDERED UNCOMMON, THE

8 PRACTITIONER OR THE OTHER DOCTOR IN THE MEDICAL

9 CENTER WANTS TO KNOW IF I, IN FACT, AGREE THAT IT

10 IS A CARCINOID PATIENT. THAT WOULD BE ONE REASON

11 THAT THEY WOULD SEND THE PATIENT TO ME. THEY'RE

12 SURPRISED TO SOMETIMES -- SOMEWHAT SURPRISED TO

13 COME UP WITH THE DIAGNOSIS AND WONDER IF IT IS

14 INDEED THAT I AGREE WITH IT.

15 THE OTHER WOULD BE THEY WOULD WANT TO

16 KNOW MY THOUGHTS ABOUT HOW THE PATIENT, IF I DO

17 AGREE WITH IT, CAN BEST BE TREATED IN THE FUTURE

18 OR FUTURE MANAGEMENT.

19 BY MS. WALTERS:

20 Q. HAVE YOU EVER DISAGREED WITH A DIAGNOSIS OF

21 OR HISTOLOGIC DIAGNOSIS OF CARCINOID IN A CASE

22 THAT'S BEEN REFERRED TO YOU CARRYING THAT

23 DIAGNOSIS?

24 A. HAVE I EVER DISAGREED WITH THE HISTOLOGICAL

25 -- THAT WOULD BE BEYOND MY REALM OF EVIDENCE

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1 BECAUSE IT'S BEYOND MY REALM OF EXPERTISE BECAUSE
2 I'M NOT A PATHOLOGIST.
3 Q. HAVE YOU EVER DISAGREED WITH THE DIAGNOSIS
4 OF CARCINOID IN A CASE THAT HAS COME TO YOU
5 CARRYING THE HISTOLOGIC DIAGNOSIS OF CARCINOID?
6 A. SOMETIMES BASED ON CLINICAL GROUNDS, I MIGHT
7 DISAGREE WITH THE DIAGNOSIS.
8 Q. HOW OFTEN DOES THAT HAPPEN?
9 A. IT HAPPENS ONLY RARELY.
10 Q. WHEN YOU SAY "RARELY", CAN YOU QUANTIFY THAT
11 A LITTLE BETTER? DOES IT HAPPEN MORE THAN ONCE A
12 YEAR?
13 A. IT WOULD HAPPEN APPROXIMATELY ONCE A YEAR.
14 Q. AND WHAT ARE THE CLINICAL GROUNDS THAT
15 YOU'RE REFERRING TO?
16 A. THIS WOULD BE A PATIENT THAT WOULD BE
17 REFERRED TO ME WITH A THOUGHT THAT THE PATIENT HAD
18 A CARCINOID, PERHAPS BASED ON BIOPSY. THESE ARE
19 USUALLY CARCINOID TUMORS THAT ORIGINATE SOMEWHERE
20 IN THE ABDOMEN, ILEO-CARCINOIDS, LET'S SAY, AND
21 THEY'RE FOUND IN THE LIVER. AND THE PATHOLOGIST
22 LOOKS AT THE LIVER BIOPSY AND SAYS THAT'S A
23 CARCINOID. SOME OTHER TUMORS ORIGINATING IN THE
24 ABDOMEN CAN HAVE A SIMILAR APPEARANCE TO CARCINOID
25 TUMORS ON HISTOLOGICAL EXAMINATION. SO I WILL

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1 LOOK AT THE OVERALL PATIENT, X-RAY FINDINGS AND SO
2 FORTH AND SEE IF, INDEED, THE PATIENT FITS THE
3 CLINICAL PICTURE OF A CARCINOID, NOT REALLY MAKING
4 AN OPINION ABOUT THE PATHOLOGY ITSELF, WHICH I'M
5 NOT AN EXPERT IN, BUT WHETHER THE OTHER CLINICAL
6 FINDINGS WOULD FIT IN WITH IT BEING A CARCINOID.
7 Q. DOCTOR, HAVE YOU EVER DISAGREED WITH A
8 DIAGNOSIS OF CARCINOID IN A PATIENT WHO'S REFERRED
9 TO YOU CARRYING THE HISTOLOGIC DIAGNOSIS OF
10 CARCINOID OF THE LUNG?
11 A. I CAN'T RECALL -- I CAN'T RECALL DIFFERING
12 IN A PATIENT THAT CARRIED A CARCINOID DIAGNOSIS OF
13 THE LUNG IF IT'S BASED ON HISTOLOGICAL CRITERIA.
14 I CAN'T RECALL THAT. THE REASON BEING THAT
15 THERE'S MORE LIMITED THINGS IN THE LUNG THAT CAN
16 LEAD TO SUCH A HISTOLOGICAL PICTURE THAT I HAVE TO
17 CONSIDER IN THE DIFFERENTIAL DIAGNOSIS. THE
18 ABDOMEN IS MORE COMPLEX.
19 Q. HAVE YOU COVERED ALL THE TYPE OF ENDOCRINE
20 TUMORS THAT YOU TREAT?
21 (OBJECTION) MR. NORTHRIP: I OBJECT TO THE FORM.
22 I DON'T THINK YOU'VE ASKED HIM ABOUT WHAT TYPE OF
23 ENDOCRINE TUMORS HE TREATS.
24 BY MS. WALTERS:
25 Q. DOCTOR, YOU STATED YOU TREATED CARCINOIDS,

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1 PHEO --

2 A. PHEOCHROMOCYTOMAS.

3 Q. AND ADRENAL CORTICAL TUMORS. ARE THERE ANY

4 OTHER TYPES OF ENDOCRINE TUMORS THAT ARE REFERRED

5 TO YOU OR THAT YOU TREAT?

6 A. YES. IN MY CAPACITY AS THE CHIEF OF

7 ENDOCRINOLOGY AT THE DURHAM V.A. MEDICAL CENTER,

8 I'LL TREAT ALL SORTS OF OTHER ENDOCRINE TUMORS.

9 THESE INCLUDE PARATHYROID ADENOMAS AND

10 HYPERPLASIA, THYROID NODULES, ISLET TUMORS OF THE

11 PANCREAS SUCH AS INSULINOMAS, GLUCAGONOMAS,

12 PITUITARY GLAND TUMORS. IN OTHER WORDS, ANY TUMOR

13 THAT CAN ARISE FROM ANY OF THE ENDOCRINE TISSUES

14 IN MY CAPACITY AS CHIEF OF ENDOCRINOLOGY AND

15 METABOLISM AT THE V.A. HOSPITAL BECAUSE THERE I'M

16 THE GENERAL ENDOCRINOLOGIST.

17 Q. WHAT PERCENTAGE OF THE PATIENTS THAT YOU SEE

18 ON AN ANNUAL BASIS HAVE AN ENDOCRINE TUMOR OF THE

19 LUNG?

20 A. I CAN'T REALLY GIVE YOU A PERCENTAGE. I CAN

21 GIVE YOU AN ESTIMATE OF NUMBERS BUT I COULDN'T

22 OFFHAND, WITH ALL THE VARIETY OF TUMORS I SEE BOTH

23 AT THE V.A. AND DUKE, COME UP WITH AN ESTIMATE.

24 Q. WHY DON'T YOU GIVE ME AN ESTIMATED NUMBER

25 THEN?

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1 A. NOW, THERE'S TWO WAYS I SEE PATIENTS WITH
2 TUMORS OF THE LUNG. THE FIRST WAY IS IN MY DUTIES
3 AS A GENERAL INTERNIST, I MAKE ATTENDING ROUNDS
4 AND AM RESPONSIBLE FOR ATTENDING ROUNDS FOR SIX
5 WEEKS OF THE YEAR, IN WHICH CASE I MAKE THE ROUNDS
6 ON A GENERAL INTERNAL MEDICINE WARD.
7 Q. IS THIS PART OF YOUR TEACHING CAPACITY?
8 A. THIS WOULD BE PART OF MY TEACHING AND
9 PATIENT CARE, ACTUALLY, CAPACITY BECAUSE I'M THE
10 RESPONSIBLE PHYSICIAN OF RECORD FOR THESE PATIENTS
11 AT THE V.A. HOSPITAL WHILE I'M MAKING THESE
12 ATTENDING ROUNDS. I'M THE LEGALLY-RESPONSIBLE
13 PHYSICIAN. SO IT'S BOTH IN THAT CAPACITY AS THEIR
14 PHYSICIAN AND AS A TEACHER OF THE RESIDENTS.
15 Q. BUT YOU WOULD ONLY BE THEIR PHYSICIAN FOR
16 SIX WEEKS; IS THAT CORRECT?
17 A. YES, FOR THE GENERAL INTERNAL MEDICINE
18 ROUNDS. IT CAN VARY FROM FIVE TO SEVEN BUT ON THE
19 AVERAGE OF SIX WEEKS DEPENDING ON WHAT TIME OF THE
20 YEAR YOU GET IT.
21 Q. AND WHAT'S THE OTHER WAY YOU GET LUNG TUMOR
22 PATIENTS?
23 A. THE OTHER WAY I WOULD GET LUNG TUMOR
24 PATIENTS WOULD BE IN MY CAPACITY AS AN EXPERT ON
25 ENDOCRINE TUMORS RATHER THAN AS A GENERAL

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1 INTERNIST, AND THEN I MIGHT BE CALLED OR I'M
2 CALLED BECAUSE THERE'S A QUESTION OF WHETHER A
3 PATIENT WITH A LUNG TUMOR HAS, IN FACT, A
4 CARCINOID TUMOR.
5 Q. AND THAT'S WHAT WE DISCUSSED EARLIER, ISN'T
6 IT?
7 A. YES, IT IS.
8 Q. AS PART OF A GROUP OF PATIENTS THAT'S
9 REFERRED TO YOU?
10 A. IT'S A SUBSET OF A GROUP OF PATIENTS WE
11 DISCUSSED EARLIER THAT HAD CARCINOID TUMORS AND
12 THIS WOULD BE A GROUP WITHIN THE CARCINOID TUMORS
13 THAT HAD CARCINOID TUMORS ORIGINATING IN THE
14 LUNG. SO THEY WOULD BE IN THERE.
15 Q. DO YOU ALSO GET ENDOCRINE TUMORS OF THE LUNG
16 AS A PRIMARY TREATING PHYSICIAN?
17 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
18 BY MS. WALTERS:
19 Q. IN YOUR CAPACITY AS A PRIMARY TREATING
20 PHYSICIAN, OTHER THAN ON THE GENERAL ROUNDS?
21 A. NOW, I'M SORRY. I DON'T UNDERSTAND EXACTLY
22 THE QUESTION ON THAT.
23 Q. YOU SAID YOU SEE PATIENTS WITH ENDOCRINE
24 TUMORS OF THE LUNG TWO WAYS; ONE, AS GENERAL
25 ROUNDS AT THE V.A. HOSPITAL DURING THE SIX-WEEK

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1 PERIOD --

2 A. NO. THAT'S NOT ENDOCRINE TUMORS OF THE

3 LUNG. I SEE PATIENTS WITH ALL KINDS OF TUMORS IN

4 THE LUNG IN THAT CAPACITY.

5 Q. OKAY. AND THAT WOULD INCLUDE ENDOCRINE

6 TUMORS?

7 A. IT MIGHT INCLUDE ENDOCRINE TUMORS, BUT

8 BECAUSE THEY MAKE UP A SMALL PROPORTION OF THE

9 LUNG TUMORS, A MAJORITY OR OTHER TYPES, BUT THEY

10 MIGHT INCLUDE ENDOCRINE JUST COINCIDENTALLY.

11 Q. AND YOU ALSO ARE REFERRED CASES OF POTENTIAL

12 OR DIAGNOSED ENDOCRINE TUMORS OF THE LUNG IN YOUR

13 CONSULTATION CAPACITY?

14 A. THAT IS CORRECT.

15 Q. ARE YOU ALSO -- DO YOU ALSO TREAT ENDOCRINE

16 TUMORS OF THE LUNG AS A PRIMARY ONGOING TREATING

17 PHYSICIAN OTHER THAN IN A CONSULTATION CAPACITY?

18 A. I WILL TREAT -- I WILL ACT AS A PRIMARY

19 PHYSICIAN FOR SOME OF THE PATIENTS AT THE V.A.

20 MEDICAL CENTER THAT HAVE CARCINOID TUMORS OF THE

21 LUNG. SOMETIMES THE ONCOLOGISTS WILL ACT AS THE

22 PRIMARY, BUT SOMETIMES AT THE V.A., I WILL ACT AS

23 A PRIMARY ALSO, DEPENDING ON THE PATIENT AND HOW

24 THEY HAPPEN TO COME INTO THE SYSTEM.

25 Q. HOW ABOUT AT DUKE?

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1 A. AT DUKE, I DO NOT ACT AS THE PRIMARY
2 TREATING PHYSICIAN FOR ANY PATIENTS WITH TUMORS OF
3 THE LUNG. I ACT AS A CONSULTANT AND ACT AS A
4 CONSULTANT TO THE ONCOLOGISTS BECAUSE OF THE WAY
5 THAT DUKE ONCOLOGY CLINICS ARE ORGANIZED.
6 Q. WHAT ARE THE TYPES OF ENDOCRINE TUMORS OF
7 THE LUNG?
8 A. ENDOCRINE TUMORS. ARE YOU REFERRING TO
9 PRIMARY OR SECONDARY?
10 Q. PRIMARY.
11 A. PRIMARY. THE MOST FREQUENT OF THE SO-CALLED
12 ENDOCRINE TUMORS OF THE LUNG WOULD BE CARCINOID
13 TUMORS OF THE LUNG AND THEIR VARIOUS GUISES,
14 TYPICAL OR ATYPICAL CARCINOID TUMORS.
15 OCCASIONALLY, THERE'S A TUMOR OF A
16 PHEOCHROMOCYTOMA THAT ARISES IN THE POSTERIOR LUNG
17 AND THE SPINAL CORD IN THE CHEST. THIS IS RATHER
18 UNCOMMON. IT'S PROBABLY A RARE PARAGANGLION OF
19 THE LUNG. THIS WOULD BE VERY, VERY UNCOMMON. SO
20 THE MAJORITY OF THE LUNGS WHICH YOU CALL ENDOCRINE
21 TUMORS WHICH ARE PRIMARY WOULD BE CARCINOID
22 TUMORS.
23 Q. IS A SMALL CELL CANCER OF THE LUNG AN
24 ENDOCRINE TUMOR OF THE LUNG?
25 A. IN GENERAL, A SMALL CELL CARCINOMA OF THE

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1 LUNG -- HOW ARE YOU DEFINING AN ENDOCRINE TUMOR,
2 IF I MIGHT ASK? WHAT ARE YOU DEFINING IT AS?
3 Q. WHY DON'T YOU DEFINE IT, DOCTOR? YOU'VE
4 BEEN USING THE TERM SO I'LL ASK YOU: WHAT IS AN
5 ENDOCRINE TUMOR?
6 A. AN ENDOCRINE TUMOR OF THE LUNG IS A TUMOR
7 WHICH SECRETES SOME USUALLY HORMONALLY-ACTIVE
8 MATERIAL FROM THE TUMOR INTO THE BLOOD STREAM OF
9 THE PATIENT. THE MATERIAL THEN TRAVELS IN THE
10 BLOOD STREAM, OTHER AREAS OF THE BODY, WHERE IT
11 WOULD EXERT A PHYSIOLOGICAL OR PHARMACOLOGICAL
12 EFFECT. THAT WOULD BE HOW I WOULD DEFINE AN
13 ENDOCRINE TUMOR OF THE LUNG.
14 Q. AND GIVE ME A COUPLE OF EXAMPLES OF
15 HORMONALLY-ACTIVE MATERIAL.
16 A. WELL, ONE HORMONALLY-ACTIVE MATERIAL WOULD
17 BE SEROTONIN. A SECOND WOULD BE
18 5-HYDROXYTRYPTOPHAN. YOU CAN ABBREVIATE 5-HTP IS
19 A SUITABLE ABBREVIATION. ANOTHER
20 HORMONALLY-ACTIVE MATERIAL THAT CAN BE SECRETED BY
21 SOME TUMORS OF THE LUNG IS AN ANTIDIURETIC
22 HORMONE, ABBREVIATED ADH, ANTIDIURETIC HORMONE.
23 ANOTHER ONE PARATHYROID- LIKE ACTIVITY, ACTH.
24 Q. ACTUALLY, THERE IS A LONG LIST OF
25 ACTIVELY-HORMONAL MATERIALS, ISN'T THERE?

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1 A. YES, BUT THERE'S CERTAIN ONES ASSOCIATED
2 WITH LUNG TUMORS AND I WAS TRYING TO GET THEM ALSO
3 COMMONLY ASSOCIATED. IT COULD BE VIRTUALLY
4 ANYTHING BUT THEY WERE ONES ON THE TOP OF THE
5 LIST. I WAS JUST GIVING YOU THE FIRST FOUR OR
6 FIVE.
7 Q. USING YOUR DEFINITION OF AN ENDOCRINE TUMOR
8 OF THE LUNG AS BEING A TUMOR THAT SECRETES
9 HORMONALLY-ACTIVE MATERIAL FROM THE TUMOR INTO THE
10 BLOOD STREAM WHICH TRAVELS AND THEN MAY EXERT A
11 PHARMACOLOGICAL EFFECT, IS A SMALL CELL CANCER OF
12 THE LUNG AN ENDOCRINE TUMOR?
13 A. UNDER CERTAIN CONDITIONS, SMALL CELL TUMORS
14 OF THE LUNG DO EXERT -- DO SECRETE
15 HORMONALLY-ACTIVE MATERIALS, AND SO WOULD QUALIFY
16 UNDER MY DEFINITION AS A HORMONALLY-ACTIVE TUMOR.
17 Q. OR ENDOCRINE TUMOR?
18 A. THERE'S TWO SENSES THAT ENDOCRINE TUMORS
19 ARISE AS USED. ONE IS THAT IT ARISES FROM AN
20 ENDOCRINE GLAND.
21 Q. I'M ONLY USING THE DEFINITION THAT YOU'VE
22 GIVEN HERE, THAT IS A TUMOR OF THE LUNG THAT
23 SECRETES HORMONALLY-ACTIVE MATERIAL FROM THE TUMOR
24 INTO THE BLOOD STREAM WHICH THEN TRAVELS AND MAY
25 EXERT A PHARMACOLOGICAL EFFECT. USING THAT

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1 DEFINITION, IS A SMALL CELL CANCER AN ENDOCRINE
2 TUMOR OF THE LUNG?
3 A. SOMETIMES -- I DON'T THINK THAT THAT'S A
4 PRECISE ENOUGH WAY TO USE AN ENDOCRINE TUMOR OF
5 THE LUNG BECAUSE IN SOME CASES, THE TUMOR OF THE
6 LUNG WILL SECRETE MATERIALS THAT THE LUNG NORMALLY
7 DOESN'T SEEM TO SECRETE IN AMOUNTS AND THAT CAN BE
8 CALLED WHAT'S CALLED A PARANEOPLASTIC SYNDROME.
9 SO IT'S SECRETING A MATERIAL BUT, IN FACT, A
10 PRECISE DEFINITION, IT'S PARANEOPLASTIC PRODUCTION
11 OF AN ENDOCRINE MATERIAL. NOW, I CALL IT A -- I
12 MIGHT CALL IT A HORMONE-SECRETING TUMOR OF THE
13 LUNG, BUT WHEN ONE BROADENS THIS, I DON'T LIKE TO
14 CALL THIS AN ENDOCRINE TUMOR OF THE LUNG. I THINK
15 THAT THAT'S A DISTORTION. IF WE'RE GOING TO USE
16 THE TERM, I'D LIKE TO USE IT IN A PRECISE WAY THAT
17 I'M USED TO USING IT.
18 Q. IS THERE A DIFFERENCE BETWEEN A
19 NEUROENDOCRINE TUMOR AND AN ENDOCRINE TUMOR?
20 A. A NEUROENDOCRINE TUMOR TENDS TO SECRETE
21 PRODUCTS WHICH ARE THOUGHT TO BE MORE FREQUENTLY
22 ASSOCIATED WITH THE NEUROENDOCRINE SYSTEM. IT
23 WOULD BE A SUBTYPE OF AN ENDOCRINE TUMOR.
24 Q. WOULD YOU CALL A SMALL CELL CANCER A
25 NEUROENDOCRINE TUMOR OF THE LUNG?

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1 A. SOME PATHOLOGISTS DO USE THAT TERMINOLOGY.
2 I DON'T USE THAT COMMONLY IN MY EVERYDAY
3 TERMINOLOGY.
4 Q. WHY IS THAT?
5 A. BECAUSE SOME SMALL CELL CARCINOMAS MAY BE
6 NEUROENDOCRINE TUMORS OF THE LUNG IN THE SENSE
7 THAT THEY SECRETE NEUROENDOCRINE PRODUCTS BUT IT'S
8 MY BELIEF, ALTHOUGH I'M NOT AN EXPERT IN THE
9 SUBJECT, THAT SOME OF THEM DO NOT SECRETE
10 NEUROENDOCRINE PRODUCTS. SO I WOULDN'T WANT TO,
11 AS AN ENDOCRINOLOGIST, IMPUGN THEM THAT THEY ALL
12 SECRETE NEUROENDOCRINE PRODUCTS SO I DON'T USE
13 THAT TERM TOO MUCH IN MY DAY-TO-DAY WORK.
14 Q. DO ALL CARCINOIDS SECRETE -- ARE CARCINOIDS
15 NEUROENDOCRINE TUMORS?
16 A. NOT ALL CARCINOIDS SECRETE IDENTIFIABLE
17 NEUROENDOCRINE PRODUCTS. I WOULD SAY THAT IT
18 DEPENDS ON ONE'S THEORIES ABOUT HOW CARCINOIDS
19 ARISE IF ONE WANTS TO SAY THEY'RE NEUROENDOCRINE.
20 AND TAKING ONE POINT OF VIEW THAT THEY CAN ARISE
21 FROM THE DIFFERENTIATION OF ADULT TISSUES, THEN
22 YOU WOULD SAY THAT THEY'RE NOT NECESSARILY
23 NEUROENDOCRINE. THIS IS BASED ON THEORIES.
24 Q. WHAT IS THE OTHER THEORY?
25 A. THE OTHER THEORY IS THAT THEY ARISE FROM

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1 NEURAL CREST TISSUE DURING EMBRYOLOGICAL LIFE, THE
2 CELLS THAT GIVE RISE TO THE CARCINOIDS. NOW, BOTH
3 OF THESE ARE AT THE PRESENT TIME JUST THEORIES.
4 Q. THAT SECOND THEORY WOULD BE IT ARISES FROM
5 THE KULCHITSKY CELL?
6 A. THAT'S RIGHT. THAT WOULD BE ONE OF THE
7 THEORIES THAT THE CARCINOID TUMORS ARISE FROM THE
8 KULCHITSKY CELL, AND THE QUESTION IS WHAT'S THE
9 THEORY ABOUT WHERE THE KULCHITSKY CELL ARISES
10 FROM. SOME WOULD SAY IT ARISES FROM THE NEURAL
11 CREST, N-E-U-R-A-L C-R-E-S-T. OTHERS WOULD SAY
12 THAT IT COULD ARISE FROM THE GERM LAYERS IN THE
13 ADULT OR THE TISSUES WITHIN THE ADULT THAT'S
14 CALLED THE MULTI-POTENTIAL TISSUES IN THE ADULT
15 TISSUES THAT YOU COULD ARISE THIS GROUP OF CELLS
16 WHICH ARE THE KULCHITSKY CELLS. BUT THESE ARE
17 THEORIES, THOUGH.
18 Q. DO YOU SUBSCRIBE TO EITHER ONE OF THESE
19 THEORIES?
20 A. ACTUALLY, I DON'T KNOW WHICH IS THE CORRECT
21 THEORY. SOMETIMES THE THEORIES ARE HELPFUL IN
22 ORGANIZING A TALK OR ONE'S THOUGHTS ON THESE
23 SUBJECTS, BUT I ALWAYS POINT OUT TO MY AUDIENCE
24 THAT, IN FACT, I DON'T KNOW IF THESE THEORIES ARE,
25 IN FACT, CORRECT. THEY'RE USEFUL SORT OF

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1 GUIDELINES TO ONE'S THINKING. BUT THE ULTIMATE
2 ANSWER ABOUT WHETHER THEY'RE, IN FACT, CORRECT IS
3 NOT IN AND HASN'T BEEN ESTABLISHED.
4 Q. I BELIEVE YOU STATED THAT NOT ALL CARCINOIDS
5 SECRETE IDENTIFIED NEUROENDOCRINE PRODUCTS?
6 A. THAT IS CORRECT.
7 Q. DO ALL CARCINOIDS SECRETE IDENTIFIED
8 ENDOCRINE PRODUCTS?
9 A. NO.
10 Q. IN THE SENSE THAT I'VE JUST STATED, ARE
11 NEUROENDOCRINE PRODUCTS AND ENDOCRINE PRODUCTS THE
12 SAME THING?
13 A. NO.
14 Q. WHAT'S THE DIFFERENCE BETWEEN AN
15 NEUROENDOCRINE PRODUCT AND AN ENDOCRINE PRODUCT?
16 A. A NEUROENDOCRINE PRODUCT, WHAT'S INCLUDED
17 UNDER A NEUROENDOCRINE PRODUCT, CAN DEPEND ON A
18 PERSON'S DEFINITION. SO, FOR INSTANCE, PRODUCTS
19 THAT ARE FOUND IN THE NERVOUS SYSTEM, HAVE BEEN
20 IDENTIFIED IN THE NERVOUS SYSTEM IN LARGE AMOUNTS
21 OR SUBSTANTIAL AMOUNTS, ARE THOUGHT OF TO BE
22 NEUROENDOCRINE PRODUCTS. THESE WOULD INCLUDE
23 THINGS LIKE NOREPINEPHRINE, SEROTONIN, SUBSTANCE
24 P, NEUROTENSIN, AND SO FORTH. THOSE WOULD BE THE
25 MAIN SORTS OF NEUROENDOCRINE PRODUCTS THAT I MIGHT

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1 DEAL WITH. ENDOCRINE PRODUCTS CAN BE THYROID
2 HORMONES, CORTISOL, PARATHYROID HORMONES, ALL THE
3 THINGS THAT THE ENDOCRINE GLANDS MAKE THAT ARE NOT
4 NORMALLY FOUND IN NEURAL TISSUES.
5 Q. CAN SEROTONIN ALSO BE AN ENDOCRINE PRODUCT?
6 A. WELL, IF YOU'RE USING ENDOCRINE IN THE SENSE
7 THAT IT IS SECRETED NOT THROUGH A DUCT BUT
8 DIRECTLY INTO THE BLOOD STREAM, IT COULD BE AN
9 ENDOCRINE PRODUCT. BUT BECAUSE IT HAS BEEN
10 ASSOCIATED WITH NEURAL TISSUE, IT'S USUALLY
11 THOUGHT OF BEING MORE THAN OF AN ENDOCRINE
12 PRODUCT.
13 Q. BUT THAT DEPENDS ON WHICH THEORY THAT YOU
14 SUBSCRIBE TO, RIGHT?
15 A. NOT NECESSARILY. DESPITE WHAT THEORY YOU
16 SUBSCRIBE TO -- IN SOME OF ITS CAPACITY, SEROTONIN
17 WOULD NOT NECESSARILY BE SECRETED AS AN ENDOCRINE
18 PRODUCT. FOR INSTANCE, IT'S FOUND IN THE WALL OF
19 THE INTESTINE WHERE IT MAY HAVE A LOCAL EFFECT.
20 Q. DOCTOR, I THINK WE'RE TALKING ABOUT LUNG
21 CANCERS HERE, LUNG TUMORS, RATHER?
22 A. OKAY.
23 MR. SIRRIDGE: ALTHOUGH WE WENT FOR A
24 LONG TIME WITHOUT SPECIFYING WHAT WE WERE TALKING
25 ABOUT.

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1 BY MS. WALTERS:

2 Q. ALL MY QUESTIONS WERE SPECIFYING LUNG

3 TUMORS.

4 A. TRY THE LAST QUESTION ANOTHER TIME IF YOU

5 CAN. JUST REPHRASE IT OR READ IT BACK.

6 Q. I HAD ASKED YOU WHETHER SEROTONIN IS AN

7 ENDOCRINE PRODUCT?

8 MR. NORTHRIP: AS A LUNG CANCER?

9 THE WITNESS: AS A LUNG CANCER?

10 BY MS. WALTERS:

11 Q. YES, RIGHT.

12 A. I WOULD SAY IT COULD BE AND IT MIGHT NOT

13 BE. I WOULD SAY IT MIGHT BE AND MIGHT NOT BE.

14 Q. BUT SEROTONIN WOULD BE A NEUROENDOCRINE

15 PRODUCT WHEN WE ARE TALKING ABOUT LUNG TUMORS?

16 A. AGAIN, I WOULD SAY IT MIGHT BE AND IT MIGHT

17 NOT BE NEUROENDOCRINE. IT MIGHT BE OR MIGHT NOT

18 BE ENDOCRINE, DEPENDING ON HOW HIGH A

19 CONCENTRATION IS FOUND. SOMETIMES IT MIGHT JUST

20 BE A LOCAL TISSUE COMPONENT THAT ISN'T AT LEAST BY

21 ALL WAYS WE CAN MEASURE IT SECRETED. SO THEN I

22 WOULDN'T CALL IT AN ENDOCRINE BECAUSE IT DOESN'T

23 GO INTO THE BLOOD STREAM THAT WE CAN MEASURE.

24 Q. HOW MANY SMALL CELL -- STRIKE THAT

25 QUESTION.

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1 DO YOU SEE ANY SMALL CELL CANCER OF YOUNG
2 PATIENTS ON AN ANNUAL BASIS?
3 A. I SEE SMALL CELL CARCINOMA PATIENTS IN MY
4 ROLE AS A GENERAL INTERNIST. PARTICULARLY AT THE
5 V.A. HOSPITAL, I WOULD SEE SMALL CELL CARCINOMA
6 PATIENTS JUST AS THEY COME IN UNSELECTED.
7 Q. THAT WOULD BE WHEN YOU'RE ON YOUR SIX-WEEK
8 ROUNDS?
9 A. SIX-WEEK ROUNDS.
10 Q. SO SIX WEEKS OUT OF THE YEAR, YOU WOULD SEE
11 SMALL CELL CANCER OF THE LUNG IN PATIENTS?
12 A. WELL, I ALSO SEE -- MIGHT SEE THEM IN MY
13 CAPACITY AS A CONSULTANT ON CARCINOID TUMORS
14 BECAUSE SOMETIMES, AND THIS IS MY CAPACITY BOTH AT
15 DUKE AND THE V.A. AS A CONSULTANT ON CARCINOID
16 TUMORS, BECAUSE SOMETIMES THERE IS A QUESTION IF
17 THE TUMOR IS A SMALL CELL TUMOR OR IF IT'S A
18 CARCINOID TUMOR.
19 IF IT TURNS OUT THAT THE DECISION IS MADE
20 THAT IT'S MOST LIKELY A SMALL CELL TUMOR, I
21 WOULDN'T SEE NECESSARILY THAT PATIENT ON A
22 CONTINUING BASIS. IF IN A PATIENT IT WAS DECIDED
23 IT'S A CARCINOID TUMOR, I WOULD PROBABLY CONTINUE
24 TO ACT AS A CONSULTANT ON THAT PATIENT. THE V.A.
25 PATIENTS I WOULD ACT ON AS A CONSULTANT AS LONG AS

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1 THEY ARE IN THE HOSPITAL AND I'M ASSIGNED TO THE
2 CLINICAL SERVICE. SO THERE'S TWO DIFFERENT HATS I
3 WEAR.
4 Q. BUT YOU'RE ONLY ASSIGNED TO THE CLINICAL
5 SERVICE FOR SIX WEEKS OUT OF THE YEAR; IS THAT
6 CORRECT?
7 A. THAT'S CORRECT.
8 Q. SO YOU WOULD -- YOU WOULD SEE THIS SMALL
9 CELL CANCER --
10 MR. NORTHRIP: I DON'T THINK THE
11 DOCTOR FINISHED HIS ANSWER.
12 THE WITNESS: IN ADDITION, SMALL CELL
13 TUMORS OF THE LUNG PRODUCE OTHER HORMONES WHICH,
14 IN GENERAL, ENDOCRINOLOGISTS ARE INTERESTED IN.
15 AND SO THROUGHOUT THE YEAR IN MY CAPACITY AS THE
16 CHIEF ENDOCRINOLOGIST AT THE V.A. HOSPITAL, I
17 WOULD SEE SMALL CELL CANCER PATIENTS IF THEIR
18 DOCTORS THOUGHT THEY MIGHT BE PRODUCING
19 HORMONALLY-ACTIVE MATERIALS AND THAT OCCURS
20 THROUGHOUT THE YEAR. THAT'S IN MY ROLE AS THE
21 ENDOCRINOLOGIST AT THE V.A. HOSPITAL.
22 BY MS. WALTERS:
23 Q. ARE SMALL CELL CANCER PATIENTS EVER REFERRED
24 TO YOU FOR SYMPTOMS OF FLUSHING AND DIARRHEA?
25 A. I CANNOT RECALL A SMALL CELL CARCINOMA

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1 PATIENT THAT TURNED OUT TO HAVE A SMALL CELL
2 CARCINOMA HAVING FLUSHING OR DIARRHEA AS A
3 PERSISTENT PROBLEM. OCCASIONALLY, THEY HAVE HAD
4 DIARRHEA ASSOCIATED WITH CHEMOTHERAPY THEY'RE
5 RECEIVING AND SO FORTH. BUT I CAN'T RECALL THEM
6 HAVING THIS AS SORT OF AN ONGOING PROBLEM NOT
7 RELATED TO THEIR THERAPY AS A SIDE EFFECT OF THEIR
8 THERAPY.
9 Q. WHAT DO YOU MEAN BY "PERSISTENT PROBLEM",
10 ONGOING, PERSISTENT?
11 A. WELL, I WOULD SAY A PERSISTENT PROBLEM IS
12 ONE THAT OCCURS OVER A PERIOD OF TIME, EITHER
13 CONTINUOUSLY OR INTERMITTENTLY AND DOES NOT BEAR
14 ANY RELATIONSHIP TO THE MEDICATIONS THE PATIENT'S
15 RECEIVING OR TO INTERCURRENT ILLNESS THAT A
16 PATIENT MIGHT HAVE. IN OTHER WORDS, IT MIGHT
17 PERSIST OVER A PERIOD OF TIME AND THE PATIENT SEES
18 IT AS A PROBLEM.
19 Q. WHAT INTERCURRENT ILLNESS ARE YOU REFERRING
20 TO?
21 A. ALL OF US, PATIENTS AND DOCTORS AND SO
22 FORTH, OCCASIONALLY GET ACUTE GASTROENTERITIS AND
23 ONE HAS DIARRHEA OCCASIONALLY AND THAT IS USUALLY
24 PROBABLY A VIRAL ILLNESS. AND WHEN IT PASSES,
25 IT'S OVER. AND SOMETIMES PEOPLE GET FOOD

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1 POISONING. SOMETIMES IN A PERIOD OF STRESS THEY
2 MIGHT HAVE DIARRHEA FOR A PERIOD FROM STRESS.
3 ONCE IN AWHILE, IT'S A SIDE EFFECT OF A
4 MEDICATION. IF YOU GIVE SOMEONE COLCHICINE OR
5 SOMETHING, THEY CAN GET DIARRHEA. THAT WOULD BE
6 RELATED TO SOME EVENT AND NOT A PERSISTENT PROBLEM
7 EITHER CONTINUOUS OR INTERMITTENT.
8 Q. WHAT ABOUT FLUSHING, WHAT TYPE OF
9 INTERCURRENT ILLNESS WOULD CAUSE FLUSHING?
10 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
11 BY MS. WALTERS:
12 Q. YOU CAN ANSWER.
13 A. WHAT TYPE OF INTERCURRENT ILLNESSES? ONE
14 THING THAT CAN CAUSE FLUSHING IS NOT NECESSARILY
15 AN ILLNESS, IS MENOPAUSE-TYPE THINGS, DECREASED
16 SUDDEN -- USUALLY A SUDDEN DECREASE IN THE
17 HORMONAL BALANCE IN THE BODY OF REPRODUCTIVE
18 HORMONES, ALTHOUGH IT'S UNCLEAR WHAT HORMONE IS
19 REALLY RESPONSIBLE.
20 ANOTHER VERY COMMON CAUSE OF FLUSHING IS A
21 PATIENT THAT HAS A FEVER, IN AN ATTEMPT TO
22 DISSIPATE THE HEAT IN THEIR BODY, THE BLOOD IS
23 SHUNTED TO THE SKIN AND THEY HAVE A RED APPEARANCE
24 WHICH IS DEFINED AS FLUSHING.
25 OCCASIONALLY, MEDICATION SUCH AS

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1 NITROGLYCERIN A PATIENT MIGHT TAKE FOR ANGINA CAN
2 PRODUCE FLUSHING. THOSE WOULD BE THE COMMON
3 THINGS THAT WOULD COME TO MY MIND, SORT OF
4 SELF-LIMITING WHERE WE SEEM TO KNOW THE CAUSE OF
5 THE FLUSHING.
6 Q. HOW DOES MENOPAUSE CAUSE OR WHY DOES
7 MENOPAUSE CAUSE FLUSHING?
8 A. WELL, I DON'T THINK THAT -- I DON'T THINK
9 THAT THE ANSWER TO THAT IS KNOWN. IT SEEMS TO BE
10 RELATED TO EITHER CHANGES IN THE MALE OR FEMALE
11 HORMONES IN THE BLOOD. IT SEEMS TO BE CORRELATED
12 BUT NOT NECESSARILY CAUSALLY-RELATED. IT MAY BE
13 DUE TO ALTERATIONS IN THE PITUITARY HORMONES,
14 TROPHIC HORMONES. THE PITUITARY GLAND IS UNDER
15 THE CONTROL OF THE HYPOTHALAMUS,
16 H-Y-P-O-T-H-A-L-A-M-U-S, AND IT MAY BE THAT IT'S
17 RELATED TO A DISCHARGE FROM THE HYPOTHALAMUS. SO
18 THERE'S A LOT OF POSSIBLE REASONS, AND I DON'T
19 FEEL THAT THE FINAL REASON WHY IT OCCURS HAS BEEN
20 ESTABLISHED. FREQUENTLY, IT CAN BE AMELIORATED BY
21 GIVING HORMONE REPLACEMENT BUT --
22 Q. HOW LONG DOES THE FLUSHING LAST OR IS THERE
23 ANY PATTERN WITH RESPECT TO MENOPAUSE?
24 A. IT USUALLY LASTS -- FIRST OF ALL, MANY
25 PEOPLE DON'T EXPERIENCE THE FLUSHING AT ALL, MEN

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1 AND WOMEN. ESPECIALLY IF THERE'S A SPONTANEOUS
2 MENOPAUSE, IT MAY JUST BE A VERY TRIVIAL PROBLEM.
3 IN A YOUNGER WOMEN WHO HAPPENS TO HAVE OVARIES
4 REMOVED OR IN A YOUNGER MAN WHO HAPPENS TO HAVE
5 THE TESTES REMOVED, IT CAN BE A MORE SIGNIFICANT
6 PROBLEM. FREQUENTLY --
7 Q. BUT -- I'M SORRY.
8 A. IT WOULD BE MORE STRIKING FLUSHING. MANY
9 PEOPLE WILL GET HORMONE REPLACEMENTS SO THEN IT
10 WILL GO AWAY SO YOU DON'T ALWAYS KNOW HOW LONG IT
11 WOULD LAST. BUT IN A USUAL PATIENT, IT SEEMS TO
12 GO AWAY IN A YEAR OR TWO, EVEN WITHOUT ANY HORMONE
13 REPLACEMENT, A YEAR OR TWO FOLLOWING CESSATION OF
14 THE GONADAL, G-O-N-A-D-A-L, ACTIVITY IT WILL
15 USUALLY CEASE --
16 Q. BUT I GUESS THERE'S NO HARD AND FAST RULE ON
17 THAT, IS THERE?
18 A. NO. THE ONLY THING -- THE ONLY ONE RULE
19 THAT I DO KNOW IS, THAT SEEMS TO HAVE HELD UP IN
20 MY EXPERIENCE, THAT ONCE IT GOES AWAY, IT DOES NOT
21 COME BACK AGAIN. I HAVE SEEN THAT IN MY CLINICAL
22 EXPERIENCE ALMOST WITHOUT EXCEPTION THAT WHEN IT
23 GOES AWAY, IT'S GONE, THE FLUSHING WILL BE GONE AS
24 THAT BEING A CAUSE.
25 Q. NOW, DESCRIBE FOR ME WHAT FLUSHING IS

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1 CLINICALLY.

2 A. OKAY. FLUSHING IS EITHER A SYMPTOM OR A

3 SIGN MANIFESTED BY REDNESS OF THE SKIN. WHEN I

4 SAY IT'S EITHER A SYMPTOM OR A SIGN, A SYMPTOM IS

5 SOMETHING A PATIENT WILL COMPLAIN OF. THEY WILL

6 SAY I'M HOT AND I LOOK IN THE MIRROR AND I'M RED.

7 A SIGN IS THAT THE PATIENT IS NOT REALLY VERY

8 AWARE THAT THEY'RE RED BUT THEIR FAMILY MAY NOTICE

9 IT OR THEIR PHYSICIAN MAY NOTICE IT. IT'S DUE TO

10 INCREASED GENERAL -- GENERALLY, IT'S DUE TO

11 INCREASED BLOOD FLOW TO THE SURFACE OF THE SKIN IS

12 THE PHYSIOLOGICAL BASIS OF THE FLUSHING, FOR

13 WHATEVER REASON.

14 Q. WHAT PARTS OF THE BODY ARE RED?

15 A. USUALLY, THE MOST COMMON AREA THAT'S RED IS

16 THE FACE, CHEEKS, THE FOREHEAD, THE CHIN. THE

17 SECOND MOST COMMON AREA IS THE "V" AREA, "V" LIKE

18 IN VICTORY, OF THE NECK AND THE UPPER PART OF THE

19 CHEST. BUT IN SEVERE FLUSHING, IT COULD INVOLVE

20 THE ENTIRE THORAX, ARMS, LEGS AND SO FORTH.

21 Q. IS IT USUALLY -- IS THE FACE -- WHEN YOU SAY

22 "FACE, CHECKS, FOREHEAD AND CHIN", THAT WOULD ALL

23 BE RED AT THE SAME TIME USUALLY?

24 A. FACE, CHEEKS, FOREHEAD AND CHIN -- WELL, THE

25 FACE WOULD INCLUDE THE CHEEKS, THE FOREHEAD AND

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1 THE CHIN SO --

2 Q. SO THAT WHOLE AREA WOULD BE RED?

3 A. GENERALLY, ALTHOUGH SOMETIMES IN PEOPLE IT'S

4 MORE IN THEIR CHEEKS. THERE MUST BE SOME KIND OF

5 ANATOMICAL REASON, BUT GENERALLY THE MOST

6 SENSITIVE AREA IS THE FACE WITH THE NECK AND THE

7 EXPOSED AREA FOR SOME REASON WHERE OPEN COLLARS GO

8 ALONG WITH THE FACE.

9 Q. SO THE NECK AND THE FACE GO TOGETHER?

10 A. I THINK THEY GO TOGETHER PRETTY MUCH.

11 Q. IN GENERAL, WOULD YOU FIND A RED NECK IN THE

12 "V" AREA AND UPPER CHEST WITHOUT HAVING A RED

13 FACE?

14 A. THAT WOULD BE VERY UNCOMMON. OF COURSE, ONE

15 HAS TO RULE OUT CAUSES OF REDNESS, SUCH AS SUN

16 EXPOSURE AND THINGS, SUNBURN AND THINGS LIKE

17 THAT. I MEAN THAT'S A FLUSHING BUT IT'S IN

18 RESPONSE TO THE TRAUMA OF THE SKIN BY THE SUN.

19 Q. WHEN YOU SAY THE "V" AREA OF THE NECK,

20 YOU'RE TALKING ABOUT A "V" AS IN THE COLLAR OF THE

21 SHIRT WHERE A "V" WOULD FORM IN THE FRONT OF THE

22 CHEST?

23 A. YES, RIGHT, "V" LIKE IN QUOTATION MARKS.

24 Q. DOCTOR, HOW MANY SMALL CELL CANCER PATIENTS

25 WOULD YOU TREAT AS A GENERAL INTERNIST AT THE V.A.

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1 HOSPITAL DURING YOUR SIX-WEEK ROUNDS IN A GIVEN
2 YEAR?
3 A. WELL, THIS IS AN ESTIMATE. MY ESTIMATE IS
4 THAT I SEE PROBABLY IN THAT SIX WEEKS 25 PATIENTS
5 WITH PRIMARY LUNG TUMORS, AND, IN GENERAL, THE
6 SMALL CELL CARCINOMAS MAKE UP ABOUT 25, 30 PERCENT
7 OF THE TOTAL LUNG TUMOR PATIENTS AT THE V.A.
8 HOSPITAL. SO I WOULD SAY IT WOULD BE SOMETHING
9 LIKE SIX OR SO PATIENTS WITH SMALL CELL CARCINOMA
10 IN MY CAPACITY AS A GENERAL INTERNIST, SIX
11 PATIENTS AS AN ESTIMATE.
12 Q. IS THAT 25 TO 30 PERCENT OF THE TOTAL
13 SOMETHING THAT HOLDS TRUE AS FAR AS YOU KNOW IN
14 THE LITERATURE AS A WHOLE?
15 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM OF
16 THE QUESTION.
17 THE WITNESS: WELL, I CERTAINLY DO
18 NOT SET MYSELF UP AS AN EXPERT ON SMALL CELL
19 CARCINOMA. SO I'M NOT -- I HAVE A GENERAL
20 KNOWLEDGE OF THE LITERATURE BUT I DON'T HAVE A
21 DETAILED KNOWLEDGE OF THE LITERATURE. DUKE IS A
22 REFERRAL CENTER FOR PEOPLE WITH COMPLICATED LUNG
23 TUMORS, PARTICULARLY THOSE THAT REQUIRE
24 MULTI-AGENT CHEMOTHERAPY. SO IT MAY BE THAT THE
25 DUKE EXPERIENCE IS THAT THERE'S MORE SMALL CELL

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1 CARCINOMAS THAN THERE MIGHT BE IN A COMMUNITY
2 HOSPITAL. BUT I DON'T -- AND THOSE CASES, WE
3 ALWAYS CONSULT THE ONCOLOGISTS. WHEN I SEE THEM
4 AS A GENERAL INTERNIST, WE GET THE ONCOLOGISTS TO
5 SEE THEM TO RECOMMEND THERAPY ON THEM.
6 BY MS. WALTERS:
7 Q. IS THAT JUST AT DUKE OR IS THAT ALSO AT THE
8 V.A. HOSPITAL?
9 A. WELL NOW, I'M JUST TALKING NOW ABOUT MY
10 CAPACITY AS A GENERAL INTERNIST AT THE V.A.
11 HOSPITAL. AT DUKE, THE ONCOLOGISTS ALWAYS SEE
12 THEM AND I WOULD ONLY BE CALLED AS A CONSULTANT IF
13 THERE WAS A QUESTION ABOUT WHETHER IT WAS, IN
14 FACT, AN OAT CELL OR IT MIGHT BE A CARCINOID.
15 Q. HOW MANY PATIENTS WITH SMALL CELL CANCER OF
16 THE LUNG DO YOU SEE ON A CONSULTATION BASIS AT
17 DUKE IN A YEAR?
18 A. I WOULD ESTIMATE THAT I WOULD PROBABLY SEE
19 ABOUT SEVEN PATIENTS WITH SMALL CELL CARCINOMA OF
20 THE LUNG AT DUKE IN MY ROLE AS A CONSULTANT
21 BECAUSE THESE SEVEN WOULD TURN OUT NOT TO HAVE
22 CARCINOIDS AND THESE WERE PEOPLE WHERE THE
23 QUESTION OF CARCINOIDS HAD COME UP WITH THEIR
24 PHYSICIANS.
25 Q. HOW WOULD THESE PATIENTS TURN OUT NOT TO

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1 HAVE CARCINOIDS, HOW WOULD THE DIAGNOSIS OF SMALL
2 CELL CANCER ULTIMATELY COME ABOUT?
3 A. WELL, THE DIAGNOSIS WOULD COME ABOUT BASED
4 ON THE PATHOLOGIST'S INTERPRETATION OF EITHER A
5 BIOPSY OR A SURGICAL RESECTION OF THE TUMOR. IT
6 WOULD COME ABOUT NOT ONLY BY THE CONFIGURATION
7 THAT THE PATHOLOGIST SEES IN THE PRIMARY TUMOR BUT
8 ALSO THE ASSESSMENT AS TO WHETHER THE TUMOR IS
9 INVOLVING OTHER AREAS THAT CAN BE INVOLVED EARLY
10 BY SMALL CELL CARCINOMA.
11 Q. SUCH AS WHAT?
12 A. SUCH AS THE BONE MARROW, MEDIASTINAL AREAS,
13 MEDIASTINAL LYMPH NODES, BRAIN, LIVER AND SO
14 FORTH, IF THERE WAS EVIDENCE THAT THE TUMOR WAS IN
15 THESE AREAS. THE OTHER THING THAT WOULD
16 CONTRIBUTE TO THE DIAGNOSIS WOULD BE WHETHER OR
17 NOT THE TUMOR, IF THE QUESTION WAS WAS IT AN OAT
18 CELL VERSUS A CARCINOID, WHETHER OR NOT THE TUMOR
19 MIGHT NOT -- WHETHER OR NOT THE TUMOR IS PRODUCING
20 SEROTONIN BECAUSE IF IT'S PRODUCING SEROTONIN, IN
21 MY EXPERIENCE, THAT MAKES IT MUCH MORE LIKELY,
22 SEROTONIN, 5-HYDROXYTRYPTAMINE, MORE LIKELY THAT
23 THE TUMOR IS, IN FACT, A CARCINOID TUMOR. SO IT
24 CONTRIBUTES TO THE OVERALL CLINICAL PICTURE.
25 AND THE OTHER THING, OF COURSE, IS THE

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1 CLINICAL COURSE OF THE PATIENT. IF THE PATIENT --
2 IF AT THE TIME WE SEE THE PATIENT, IF WE'VE HAD A
3 CHANCE TO OBSERVE HIM OR IF HIS DOCTOR HAS FOR ANY
4 PERIOD OF TIME SINCE THE TUMOR WAS DISCOVERED, THE
5 CLINICAL COURSE WOULD PLAY A ROLE IN ONE'S
6 JUDGMENT ABOUT THE NATURE OF THE TUMOR.
7 Q. WOULD A DIAGNOSIS OF SMALL CELL -- WOULD A
8 HISTOLOGIC DIAGNOSIS OF SMALL CELL CANCER BE
9 CHANGED TO CARCINOID BASED ON THE FACT THAT THE
10 TUMOR IS PRODUCING SEROTONIN?
11 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM OF
12 THE QUESTION. COULD YOU READ THAT BACK?
13 (DESIGNATED QUESTION IS READ)
14 THE WITNESS: IF THE TUMOR, AND I
15 DON'T SET MYSELF UP AS AN EXPERT ON THE HISTOLOGY
16 BECAUSE I'M NOT A PATHOLOGIST, BUT IF THE TUMOR
17 HAD THE CLASSICAL APPEARANCE OF A SMALL CELL
18 CARCINOMA AS SEEN BY THE PATHOLOGIST AND HAD THE
19 CLASSICAL CLINICAL COURSE SO FAR AS A SMALL CELL
20 CARCINOMA, IT WOULD NOT NECESSARILY BE CHANGED
21 FROM ITS CLASSIFICATION AS A SMALL CELL CARCINOMA
22 IF IT WAS PRODUCING SEROTONIN.
23 HOWEVER, THE PATHOLOGISTS FREQUENTLY
24 HAVE CONSIDERABLE DIFFERENCE OF OPINION ON THE
25 NATURE OF THE TUMOR AND SOMETIMES, THE

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1 PATHOLOGIST, ONE PATHOLOGIST WOULD BE UNCERTAIN
2 BECAUSE IT'S GOT PERHAPS FEATURES OF BOTH TYPES OF
3 TUMORS IN DIFFERENT AREAS OR THEY'LL BE A
4 DIFFERENCE OF -- AN HONEST DIFFERENCE OF OPINION
5 BETWEEN TWO DIFFERENT PATHOLOGISTS. AND IN THAT
6 CASE, THE INFORMATION ABOUT WHETHER THE TUMOR
7 PRODUCED SEROTONIN BECAUSE OF ITS STATISTICAL
8 ASSOCIATION WITH CARCINOIDS WITH SEROTONIN, IN
9 THAT CASE THE INFORMATION MIGHT PLAY A ROLE IN
10 MAKING A CLINICAL DECISION ON HOW TO MANAGE THE
11 PATIENT.
12 MR. SIRRIDGE: SINCE WE'VE BEEN GOING
13 LIKE AN HOUR-AND-A-HALF --
14 MS. WALTERS: LET ME JUST ASK HIM ONE
15 MORE QUESTION.
16 BY MS. WALTERS:
17 Q. IN THAT CASE WHERE THE INFORMATION MIGHT
18 PLAY A ROLE IN THE CLINICAL DECISION ABOUT HOW TO
19 MANAGE THE PATIENT, IN THAT CASE, WOULD THE
20 INFORMATION PLAY A ROLE IN THE DIAGNOSIS OR CHANGE
21 THE DIAGNOSIS?
22 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
23 THE WITNESS: CHANGE THE DIAGNOSIS?
24 I THINK IT COULD CHANGE THE CLINICAL PROBABILITY,
25 THE CLINICAL -- WHEN THERE IS A QUESTION WHERE THE

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1 PATHOLOGISTS ARE DIVIDED IN WHAT THE TUMOR IS, I
2 THINK IT COULD CHANGE THE PROBABILITY THAT THE
3 TUMOR IS GOING TO FOLLOW THE COURSE OF EITHER A
4 CARCINOID TUMOR OR A SMALL CELL CARCINOMA, THE
5 KNOWLEDGE THAT IT PRODUCED SEROTONIN WHEN THERE IS
6 A DEBATE, AND ONE HAS TO GET WHATEVER CLINICAL OR
7 LABORATORY INFORMATION ONE CAN GET TO TRY TO MAKE
8 A DECISION IN THE PATIENT'S MANAGEMENT. I THINK
9 IT COULD -- IT WOULD HAVE AN INFLUENCE ON MY
10 DECISION IN THOSE CASES.
11 BY MS. WALTERS:
12 Q. FOR CLINICAL MANAGEMENT?
13 A. THE CLINICAL MANAGEMENT AND THE WORKING
14 DIAGNOSIS THAT I CONSIDER FOR THE TUMOR. IN OTHER
15 WORDS, THE DIAGNOSIS THAT I WANT TO ACCEPT AT THAT
16 TIME BECAUSE THE DIAGNOSIS WILL DETERMINE IN SOME
17 CASES THE THERAPY THAT'S GIVEN.
18 MS. WALTERS: LET'S TAKE A SHORT
19 BREAK.
20 (BRIEF RECESS)
21 BY MS. WALTERS:
22 Q. DOCTOR, YOU TESTIFIED JUST BEFORE THE BREAK
23 THAT YOU SEE SIX PATIENTS A YEAR WITH SMALL CELL
24 CANCER ON ROUNDS AT THE VETERANS ADMINISTRATION
25 HOSPITAL AND YOU SEE APPROXIMATELY SEVEN PATIENTS

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1 A YEAR ON A CONSULTATION BASIS AT DUKE UNIVERSITY
2 MEDICAL CENTER. ARE THERE ANY OTHER SMALL CELL
3 CANCER PATIENTS THAT YOU SEE IN THE COURSE OF A
4 YEAR, OF THE LUNG, THAT IS?
5 A. YES, RIGHT. I SEE SEVEN AT DUKE WHEN THE
6 QUESTION COMES UP IS IT AN OAT OR SMALL-CELL
7 CARCINOMA OR A CARCINOID. HOW MANY DID YOU SAY
8 THAT I STATED I SAW?
9 Q. SEVEN AT DUKE, SIX ON ROUNDS AT THE VETERANS
10 ADMINISTRATION HOSPITAL.
11 A. RIGHT, ONE-FOURTH OF THE TOTAL PATIENTS WITH
12 LUNG TUMORS. AND THEN IN ADDITION, I SEE SOME
13 PATIENTS IN MY CAPACITY AS AN ENDOCRINOLOGIST AT
14 THE V.A. THAT HAVE SOME HORMONAL MANIFESTATION
15 POSSIBLY RELATED TO THE OAT CELL THROUGHOUT THE
16 ENTIRE YEAR BECAUSE I MAKE ENDOCRINE ROUNDS THE
17 ENTIRE YEAR. AND THERE, I'LL SAY, I PROBABLY SEE
18 THREE OR FOUR MORE AS A CONSULTANT ON THESE TYPE
19 OF ENDOCRINE MANIFESTATIONS.
20 Q. AND WHAT TYPE OF -- BY "MANIFESTATION", DO
21 YOU MEAN SYMPTOMS?
22 A. EITHER SYMPTOMS OR LABORATORY FINDINGS.
23 EITHER SYMPTOMS OR LABORATORY FINDINGS.
24 Q. DO ANY OF THOSE SYMPTOMS OR LAB FINDINGS
25 RELATE TO SEROTONIN AND ITS METABOLITES?

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1 A. USUALLY, IN THAT CAPACITY AS A GENERAL
2 ENDOCRINOLOGIST AT THE V.A., THE SYMPTOMS OR THE
3 FINDINGS ARE RELATED TO INAPPROPRIATE SECRETION OF
4 AN ANTIDIURETIC HORMONE OR MORE UNCOMMONLY TO
5 SECRETION OF ACTH BY THE TUMOR, ACTH, AND THAT'S
6 IN THAT CAPACITY.
7 Q. AND THOSE THREE ARE FOR OAT CELL PATIENTS
8 THAT ARE REFERRED TO YOU ARE REFERRED FOR
9 MANAGEMENT OF THOSE SYMPTOMS?
10 A. THEY ARE REFERRED FOR RECOMMENDATIONS ABOUT
11 DO THEY HAVE THIS PROBLEM. IF THEY DO HAVE IT, IS
12 IT RELATED TO THE SMALL CELL CARCINOMA OR COULD IT
13 BE RELATED TO SOMETHING ELSE AND WHAT'S THE BEST
14 WAY TO TREAT THE PATIENTS WITH THESE PROBLEMS, OUR
15 RECOMMENDATIONS IN OUR ROLE, AND OUR ROLE IS
16 GENERAL CONSULANTS IN ENDOCRINOLOGY AT THE V.A.
17 MEDICAL CENTER.
18 Q. I TAKE IT FROM READING YOUR ARTICLES THAT AS
19 A GENERAL PRACTICE, ANY PATIENT AT THE DUKE
20 MEDICAL CENTER THAT IS DIAGNOSED AS HAVING OR
21 SUSPECTED OF HAVING A CARCINOID TUMOR OF THE LUNG
22 IS AUTOMATICALLY TESTED FOR SEROTONIN AND OTHER
23 SUBSTANCES?
24 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
25 (OBJECTION) MR. NORTHRIP: OBJECT TO THE FORM.

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1 BY MS. WALTERS:

2 Q. IS THAT CORRECT?

3 MR. SIRRIDGE: WOULD YOU READ THE

4 QUESTION BACK?

5 MR. NORTHRIP: I DON'T KNOW WHETHER

6 YOU TAKE IT FROM READING THE ARTICLES OR NOT.

7 THAT'S MY PORTION OF THE OBJECTION.

8 MS. WALTERS: I'LL STICK WITH THE

9 QUESTION.

10 MR. SIRRIDGE: READ IT BACK.

11 (DESIGNATED QUESTION IS READ)

12 THE WITNESS: CARCINOID TUMOR OF THE

13 LUNG?

14 BY MS. WALTERS:

15 Q. CORRECT.

16 A. I WOULD SAY THAT THAT'S NOT CORRECT.

17 Q. ARE PATIENTS THAT HAVE BEEN DIAGNOSED AS

18 HAVING CARCINOID TUMOR OF THE LUNG AUTOMATICALLY

19 TESTED FOR SEROTONIN AT THE DUKE MEDICAL CENTER?

20 A. NOT AUTOMATICALLY.

21 Q. WHEN WOULD THEY BE TESTED?

22 A. WELL, THEY WOULD BE TESTED IF THEIR PRIMARY

23 PHYSICIAN ORDERED THE TESTS AND HE CAN ORDER THE

24 5-HIAA TEST FROM THE DUKE HOSPITAL LABORATORY. SO

25 HE COULD JUST ON HIS OWN GO AHEAD AND ORDER THAT

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1 TEST. THE OTHER THING THAT HE COULD DO WOULD BE
2 TO CALL ME AND ASK ME TO CONSULT ON THE CASE. AND
3 AS PART OF THE CONSULTATION, I ANALYZE URINE IN MY
4 LABORATORY, NOT ONLY FOR THE 5-HIAA, BUT ALSO FOR
5 SEROTONIN. SOMETIMES BLOOD SEROTONIN. BUT THIS
6 WOULD NOT HAPPEN AUTOMATICALLY. THE DOCTOR MAY
7 CHOOSE NOT TO ORDER THE TESTS OR NOT TO CALL ME.
8 Q. IS IT TRUE THAT ALL PATIENTS WITH CARCINOID
9 TUMOR OF THE LUNG THAT ARE EITHER REFERRED TO YOU
10 -- WELL, NOT EITHER, THAT ARE REFERRED TO YOU ON A
11 CONSULTATION BASIS AT DUKE MEDICAL CENTER, DO YOU
12 AUTOMATICALLY TEST FOR SEROTONIN AND ITS
13 METABOLITES?
14 A. ALL PATIENTS THAT ARE REFERRED TO ME I TRY
15 TO TEST FOR SEROTONIN AND METABOLITES. RARELY, A
16 PATIENT BY THE TIME I HEAR ABOUT THEM WOULD BE
17 SCHEDULED FOR DISCHARGE AND I COULDN'T GET A
18 24-HOUR URINE. I MIGHT BRING IT BACK OR I MIGHT
19 JUST GET A BLOOD SAMPLE, BUT I MAKE A STRONG
20 ATTEMPT TO TEST ALL PATIENTS I'M CONSULTED ON
21 WITHIN THOSE CONSTRAINTS.
22 Q. WHY IS THAT?
23 A. WHY DO I DO IT?
24 Q. YES.
25 A. I DO IT BECAUSE I FEEL THAT IT'S GOOD

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1 MEDICAL PRACTICE FOR ALL PATIENTS WHO HAVE HAD A
2 DIAGNOSIS OF CARCINOID TUMOR, EVEN IF THE TUMOR
3 HAS BEEN RESECTED, TO ESTABLISH WHAT THEIR LEVEL
4 OF SEROTONIN PRODUCTION AND 5-HIAA SECRETION IS
5 AFTER SURGERY SO THAT ONE CAN USE THAT INFORMATION
6 FOR FUTURE FOLLOW-UP OF THE PATIENT TO DETERMINE
7 IF AT A LATER DATE THE VALUE SHOULD BE NORMAL AND
8 AT A LATER DATE IT SHOULD INCREASE, THAT WOULD
9 SUGGEST THAT THE TUMOR MAY BE COMING BACK. SO I
10 FEEL LIKE YOU SHOULD HAVE A POSTOPERATIVE VALUE OF
11 THESE THINGS WOULD BE THE GOOD PRACTICE -- THE
12 BEST CLINICAL PRACTICE IN DEALING WITH PATIENTS
13 WITH CARCINOID TUMORS OF ALL TYPES.
14 Q. SO THEN WITH RESPECT TO THE CARCINOID TUMORS
15 THAT YOU SEE ON A CONSULTATION BASIS AT DUKE, ARE
16 MOST OF THEM TESTED AFTER SURGERY?
17 A. MOST OF THEM WOULD BE TESTED AFTER SURGERY
18 BUT BECAUSE I DON'T HAVE TOTAL CONTROL, I'M A
19 CONSULTANT, THERE ARE OCCASIONAL ONES THAT THE
20 DOCTOR WOULD DISCHARGE AND ELECT NOT TO TEST THEM.
21 Q. HOW MANY OF THESE PATIENTS THAT YOU SEE ON A
22 CONSULTATION BASIS HAVE HAD SEROTONIN TESTS BEFORE
23 SURGERY?
24 A. WHEN DEALING WITH THE BRONCHIAL CARCINOID
25 TUMORS, A SMALL PERCENTAGE ONLY HAVE HAD THE

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1 CARCINOID TUMORS -- THE 5-HIAA MEASUREMENTS BEFORE
2 SURGERY BECAUSE IN MANY CASES, THE CARCINOID TUMOR
3 IS NOT RECOGNIZED UNTIL SURGERY IS DONE AND THE
4 TUMOR IS REMOVED AND IT'S RECOGNIZED IT'S A
5 CARCINOID TUMOR. AND I WOULD, YOU KNOW, I WOULD
6 SAY IT'S A SMALLER, DEFINITELY A SMALLER MINORITY
7 OF PATIENTS. OCCASIONALLY, THE BRONCHOSCOPY
8 SUGGESTS THE BRONCHIAL TUMOR BY A BRONCHIAL
9 BIOPSY, AND THEN PRIOR TO SURGERY, I MAY BE
10 CONSULTED TO ANALYZE URINE, BUT SOMETIMES IF
11 THERE'S NOT A SUGGESTION OF A BRONCHOSCOPY, THEN
12 THEY MAY HAVE THE TUMOR REMOVED BEFORE IT'S
13 RECOGNIZED WHAT IT IS OR WHAT IT MIGHT BE.
14 Q. WITH RESPECT TO THE SMALL CELL CANCER
15 PATIENTS THAT YOU SEE, THE SEVEN ON CONSULTATION
16 AT DUKE AND THE SIX ON ROUNDS AT THE VETERANS
17 ADMINISTRATION HOSPITAL, HOW MANY OF THESE WOULD
18 BE TESTED FOR SEROTONIN PRODUCTION?
19 A. WELL, IN GENERAL, THE SEVEN THAT I SEE AT
20 THE V.A. AT THE PRESENT TIME WOULD NOT BE TESTED
21 FOR -- OKAY. REREAD ME THE QUESTION. I WANT TO
22 MAKE SURE WHAT WE'RE TALKING ABOUT, IF YOU COULD.
23 (DESIGNATED QUESTION IS READ)
24 THE WITNESS: OKAY. THE PATIENTS I
25 SEE AT DUKE WOULD PROBABLY ALL BE TESTED BECAUSE

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1 IN THAT CASE, THERE WAS SOME REASON TO SUSPECT A
2 CARCINOID TUMOR VERSUS THE SMALL CELL TUMOR AND
3 I'M TRYING TO USE THE SEROTONIN TO HELP MYSELF AND
4 THE REFERRING PHYSICIAN OF A DECISION.
5 NOW, THE PATIENTS THAT ARE SEEN AS MY
6 ROUTINE DUTIES AT THE V.A. AS AN INTERNAL MEDICAL
7 SPECIALIST, IN GENERAL, THEY WOULD NOT BE TESTED
8 BECAUSE THEY HAVE WHAT IS THOUGHT TO BE ACCEPTED
9 BY MYSELF AND THE OTHER PHYSICIANS TAKING CARE OF
10 THEM AND THE ONCOLOGISTS THAT THEY DO HAVE SMALL
11 CELL CARCINOMA. AND SO UNLESS I WAS DOING A
12 SPECIAL STUDY AT THE TIME, I WOULDN'T -- I WOULD
13 NOT ROUTINELY TEST THESE PEOPLE FOR SEROTONIN AND
14 ITS METABOLITES.
15 BY MS. WALTERS:
16 Q. SO YOU ONLY TEST PATIENTS THAT ARE REFERRED
17 TO YOU WITH A DIFFERENTIAL DIAGNOSIS OF SMALL CELL
18 CANCER VERSUS CARCINOID?
19 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM AS
20 MISSTATING HIS TESTIMONY.
21 THE WITNESS: COULD YOU SAY THE
22 QUESTION AGAIN, PLEASE?
23 BY MS. WALTERS:
24 Q. YOU ONLY TEST SMALL CELL CANCER PATIENTS OR
25 SUSPECTED SMALL CELL CANCER PATIENTS THAT COME TO

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1 YOU WITH A DIFFERENTIAL DIAGNOSIS OF CARCINOID?
2 (OBJECTION) MR. SIRRIDGE: I STILL OBJECT TO THE
3 FORM.
4 THE WITNESS: WELL, WHAT I'M
5 DESCRIBING FOR YOU IS WHAT I WOULD DO AT THE
6 PRESENT TIME. IN PAST YEARS, I'VE DONE STUDIES TO
7 TRY AND ESTABLISH IF IT'S WORTHWHILE TO TEST
8 PATIENTS WITH SMALL CELL CARCINOMA IRREGARDLESS OF
9 THE DIFFERENTIAL DIAGNOSIS OF SEROTONIN, AND
10 THERE'S BEEN TIMES THERE. THERE WAS ONE PERIOD OF
11 SIX WEEKS WHERE I TESTED ALL THE SMALL CELL
12 PATIENTS I SAW WHILE MAKING ROUNDS ON THESE
13 PATIENTS, IRREGARDLESS OF THE DIFFERENTIAL -- EVEN
14 IF CARCINOID WAS NOT A SERIOUS CONSIDERATION. SO
15 WHAT I'M DESCRIBING IS WHAT I WOULD HAVE DONE
16 IRREGARDLESS, LET'S SAY, WHEN I ROUNDED LAST
17 FEBRUARY. BUT FOUR YEARS AGO, I MIGHT HAVE BEEN
18 DOING SOMETHING DIFFERENT. AND AT ONE TIME, I WAS
19 DOING SOMETHING DIFFERENT.
20 BY MS. WALTERS:
21 Q. WELL, LET ME GO THROUGH THIS
22 CHRONOLOGICALLY. WHAT WERE YOU DOING UP UNTIL
23 FOUR YEARS AGO?
24 A. FROM TIME TO TIME, AND, AGAIN, I CAN'T GIVE
25 YOU THE PRECISE TIME, FROM TIME TO TIME, BECAUSE

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1 OF MY SCIENTIFIC INTEREST IN THE PROBLEM, I HAVE
2 TESTED ALL THE PATIENTS I ENCOUNTERED WITH SMALL
3 CELL CARCINOMA TO SEE IF THEY MIGHT HAVE
4 PRODUCTION OF SEROTONIN THAT WOULDN'T OTHERWISE
5 HAVE BEEN SUSPECTED. I DID THIS FOR A PERIOD OF
6 TIME IN APPROXIMATELY LATE 1978, EARLY 1979 WAS MY
7 RECOLLECTION.
8 Q. AND THESE WERE ALL PATIENTS THAT YOU WERE
9 SEEING ON A CONSULTATION BASIS AT DUKE?
10 A. NO, NO. THESE WERE PATIENTS THAT I SAW IN
11 MY ROUNDING CAPACITY AS A GENERAL INTERNIST AT THE
12 DURHAM V.A. HOSPITAL AT THE SPECIFIC TIME PERIOD
13 OF LATE '78 AND EARLY '79.
14 Q. AND WHEN WERE THESE PATIENTS -- STRIKE THAT.
15 DO YOU HAVE A RECORD OF HOW MANY PATIENTS
16 YOU TESTED?
17 A. YES, BECAUSE THE RESULTS OF THIS TESTING
18 RESULTED IN A PUBLICATION CONCERNING IT. AND
19 THAT'S THE ONLY REASON I CAN RECALL SPECIFICALLY.
20 Q. AND WHAT YEAR IS THAT PUBLICATION?
21 A. THAT PUBLICATION WAS IN 1979, AND I BELIEVE
22 YOU WOULD HAVE THAT PUBLICATION; IS THAT RIGHT,
23 MR. SIRRIDGE?
24 MR. SIRRIDGE: YES.
25 BY MS. WALTERS:

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1 Q. IS THAT THE ARTICLE THAT WAS PUBLISHED IN
2 GASTROENTEROLOGY --
3 A. NO. THAT ONE WAS ACTUALLY PUBLISHED IN THE
4 JOURNAL OF CANCER, VOLUME 44, PAGE 1751, 1979.
5 Q. WHAT'S THE TITLE OF THAT ARTICLE?
6 A. THE TITLE IS THE EFFECT OF METASTATIC CANCER
7 ON PLATELET MONOAMINE OXIDASE ACTIVITY AND
8 SEROTONIN METABOLISM.
9 MR. SIRRIDGE: PROBABLY WOULD BE
10 FACILITATED FOR YOU TO LOOK IN THAT PACK OF
11 MATERIALS THERE WITHIN THE CLIP.
12 BY MS. WALTERS:
13 Q. AND THAT'S ITEM NUMBER EIGHT THAT YOU
14 PROVIDED TO MR. SIRRIDGE IN YOUR COVER LETTER OF
15 DECEMBER 1, 1986?
16 A. YES, ITEM NUMBER EIGHT.
17 Q. HOW MANY SMALL CELL CANCER PATIENTS DID YOU
18 TEST THERE?
19 A. I TESTED 13 CONSECUTIVE PATIENTS WITH SMALL
20 CELL CARCINOMA OF THE LUNG AMONGST THE SERIES OF
21 52 CANCER PATIENTS WITH A VARIETY OF CANCERS.
22 Q. AND WHAT DID YOU TEST THEM FOR?
23 A. WELL, I TESTED THEM FOR SECRETION OF
24 5-HYDROXYINDOLEACETIC ACID, 5-HIAA, IN THEIR URINE
25 AND SEROTONIN SECRETION IN THEIR URINE, AND SOME

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1 OF THEM I ALSO TESTED FOR TRYPTAMINE IN THEIR
2 URINE, TYRAMINE IN THEIR URINE. THESE WERE OTHER
3 AMINES I'M INTERESTED IN.
4 Q. I'M TALKING SPECIFICALLY ABOUT THE SMALL
5 CELL CANCER PATIENTS.
6 MR. SIRRIDGE: WHAT ARE YOU TALKING
7 ABOUT?
8 BY MS. WALTERS:
9 Q. I'M TALKING SPECIFICALLY ABOUT THE SMALL
10 CELL CANCER OF THE LUNG PATIENTS, THOSE YOU TESTED
11 FOR 5-HIAA SEROTONIN BOTH IN THE URINE. DID YOU
12 TEST THEM FOR ANYTHING ELSE?
13 A. SOME OF THEM, AND I CAN'T SAY SPECIFICALLY
14 HOW MANY, AND I TESTED ALSO FOR TRYPTAMINE IN THE
15 URINE WHICH IS ANOTHER AMINE, TYRAMINE,
16 T-Y-R-A-M-I-N-E, IN THE URINE. AND SOME I ALSO,
17 AND I CAN'T SAY THE PRECISE NUMBER OF THE SMALL
18 CELL, I ALSO TESTED FOR AN ENZYME CALLED MONOAMINE
19 OXIDASE IN THEIR PLATELETS. IT HAPPENS TO BE
20 SOMETHING I WAS INTERESTED IN AT THE TIME. IT'S
21 M-O-N-O-A-M-I-N-E O-X-I-D-A-S-E, ABBREVIATED MAO.
22 Q. AND, DOCTOR, WHAT OTHER WAYS ARE THERE TO
23 DETERMINE WHETHER SEROTONIN IS PRESENT IN A TUMOR
24 OTHER THAN TESTING FOR URINE, THE URINARY PRESENCE
25 OF SEROTONIN?

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1 A. ANOTHER WAY OF TESTING IS TO TEST FOR THE
2 LEVEL OF SEROTONIN IN THE BLOOD IN SOME COMPONENT
3 OF THE BLOOD. IT CAN BE THE BLOOD PLATELETS THAT
4 STORE SEROTONIN. IT CAN BE THE BLOOD SERUM WHERE
5 THE SEROTONIN IS RELEASED FROM THE PLATELETS WHEN
6 THE BLOOD CLOTS OR IT CAN BE THE TOTAL BLOOD,
7 AGAIN, WHERE YOU ALLOW THE BLOOD TO CLOT AND
8 MEASURE THE TOTAL SEROTONIN IN THE BLOOD. IN THAT
9 PARTICULAR STUDY, I DIDN'T STUDY THE BLOOD LEVELS
10 OF SEROTONIN IN THESE VARIOUS FORMS. I STUDIED
11 ONLY THE URINE LEVELS WHICH HAVE OVER TIME PROVED
12 TO BE ACTUALLY MORE SENSITIVE.
13 Q. WHY DIDN'T YOU STUDY THE BLOOD?
14 A. AT THE TIME I DID NOT HAVE -- AT THE TIME
15 ONE OF THE REASONS WAS THAT I DIDN'T REALLY WANT
16 TO CAUSE THE PATIENTS THE DISCOMFORT OF STICKING
17 THEM. I THOUGHT IT WOULD BE EASIER FOR THE
18 PATIENTS IF WE JUST COLLECTED THE URINE. AND,
19 ALSO, I HAD A REASON TO BELIEVE THEN, WHICH HAS
20 BEEN CONFIRMED OVER TIME, THAT ACTUALLY THE BLOOD,
21 -- THE URINE, CORRECTION, THE URINE, IS A MORE
22 SENSITIVE WAY TO DETECT SEROTONIN PRODUCTION THAN
23 IS THE BLOOD. THERE WERE TWO REASONS.
24 Q. HOW MANY TESTS DID YOU PERFORM ON EACH OF
25 THESE SMALL CELL CANCER PATIENTS, HOW MANY URINARY

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1 TESTS IN TIME SEQUENCE?

2 A. WELL, AGAIN, IT WOULD HAVE TO BE MY

3 RECOLLECTION BECAUSE IT WAS '79, BUT MY USUAL

4 PROCEDURE WOULD BE TO COLLECT ONE 24-HOUR URINE

5 AND ANALYZE IT FOR THIS ON EACH OF THE PATIENTS.

6 NOW, IF FOR SOME REASON OCCASIONALLY AN ASSAY DOES

7 NOT MEET THE STANDARDS I HAVE FOR IT OF QUALITY

8 CONTROL AND SO FORTH, IT'S POSSIBLE THAT I ANALYZE

9 THE URINE A SECOND TIME, BUT I DON'T RECALL THAT.

10 BUT IT HAD TO MEET MY STANDARDS FOR QUALITY

11 CONTROL BEFORE I WOULD ACCEPT IT AS A VALUE. BUT

12 EACH WAS ONE URINE.

13 Q. DID ANY OF THESE SMALL CELL CANCER PATIENTS

14 HAVE SURGERY?

15 A. I'M CERTAIN THAT SOME OF THEM MIGHT HAVE HAD

16 SURGERY ALTHOUGH BECAUSE OF THE TIME, I DIDN'T

17 SPECIFICALLY INCLUDE THAT IN THE PAPER AND I CAN'T

18 RECALL THAT, BUT ONE OF THE CRITERIA FOR STUDYING

19 THEM WAS THAT THEY HAD TO HAVE KNOWN SMALL CELL

20 CARCINOMA PRESENT IN THEIR BODY AT THE TIME THE

21 URINE WAS COLLECTED. IN OTHER WORDS --

22 Q. HADN'T BEEN DIAGNOSED?

23 A. THEY HAD ALL BEEN DIAGNOSED BY STANDARD

24 HISTOLOGICAL CRITERIA BY QUALIFIED PATHOLOGISTS.

25 AND MY RECOLLECTION IS THAT THERE WASN'T ANY

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1 DEBATE ABOUT WHETHER THEY, IN FACT, HAD THAT
2 DIAGNOSIS. I THINK THEY WERE ALL ACCEPTED BY US
3 AT THE TIME AS BEING SMALL CELL CARCINOMA
4 PATIENTS.
5 Q. HOW MANY OF THEM HAD METASTATIC DISEASE AT
6 THE TIME YOU TESTED THEM?
7 A. HOW MANY OF THEM HAD METASTATIC DISEASE? I
8 WOULD SAY THAT THE MAJORITY HAD METASTATIC
9 DISEASE, BUT I CAN'T SAY THIS WITH CERTAINTY. I
10 HAVE A STATEMENT IN HERE ABOUT ALTHOUGH MANY OF
11 THE PATIENTS HAD INVOLVEMENT OF THE LIVER WITH
12 METASTATIC TUMORS, NONE OF THEM HAD GROSS
13 DERANGEMENTS OF LIVER FUNCTION, BUT I DON'T
14 SPECIFICALLY SEE IN HERE HOW MANY HAD METASTATIC
15 -- THE USUAL EXPERIENCE IS, THOUGH, THAT WITH
16 SMALL CELL CARCINOMAS, THE MAJORITY WOULD HAVE HAD
17 METASTATIC, BUT I CAN'T SAY THIS WITH CERTAINTY.
18 Q. DOES THE STATEMENT YOU JUST READ REFER TO
19 ALL THE CANCER PATIENTS OR JUST THE SMALL CELL
20 CANCER PATIENTS?
21 A. REFERS TO ALL THE CANCER PATIENTS. YOU MEAN
22 THE QUESTION ABOUT THE LIVER?
23 Q. CORRECT.
24 A. YES. THE PURPOSE OF THAT QUESTION WAS TO
25 POINT OUT THAT THEY DIDN'T HAVE A GROSS

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1 DERANGEMENT OF LIVER FUNCTION WHICH COULD POSSIBLY
2 AFFECT THE RESULTS OF THE STUDIES. IF SOMEONE HAD
3 A REAL BAD LIVER WHERE THE LIVER IS INVOLVED IN
4 ACTIVATING SEROTONIN, THEY COULD HAVE SOME
5 DERANGEMENTS JUST DUE TO THE MASS OF LIVER, BUT
6 THEY DIDN'T HAVE THAT. THEY MAY HAVE HAD SOME BUT
7 IT WASN'T MASSIVE.
8 Q. HOW MANY OF THESE SMALL CELL CANCER PATIENTS
9 HAD AN ACTIVE DISEASE AT THE TIME THAT YOU TESTED
10 THEM?
11 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM OF
12 THE QUESTION. I HAVE NO IDEA WHAT "ACTIVE"
13 MEANS.
14 BY MS. WALTERS:
15 Q. DOCTOR, DO YOU USE THE TERM "ACTIVE
16 DISEASE"?
17 A. I DON'T GENERALLY USE THE TERM "ACTIVE
18 DISEASE".
19 Q. WHAT DOES THAT MEAN TO YOU, THE TERM "ACTIVE
20 DISEASE"?
21 A. WELL, WHAT DOES IT MEAN? IT REALLY DOESN'T
22 HAVE ANY MEANING TO ME IN THE WAY I PRACTICE
23 MEDICINE. I'D HAVE TO HAVE IT DEFINED FOR ME.
24 FOR THIS PAPER, I DEFINED IT AS PEOPLE ALL HAVING
25 TUMOR PRESENT IN THEIR BODIES. BUT I DON'T KNOW

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1 EXACTLY WHAT ACTIVE -- YOU KNOW, I DON'T USE THAT
2 TERM.
3 Q. DO YOU STILL HAVE THE CLINICAL DATA ON THESE
4 PATIENTS?
5 A. I REALLY DON'T KNOW BECAUSE IT'S SO LONG
6 AGO. NO, THE CLINICAL DATA, I REALLY WOULDN'T
7 HAVE ACCESS TO THE CLINICAL DATA.
8 Q. DO YOU RECALL -- I'M SORRY. GO AHEAD.
9 A. BECAUSE THEY WERE PEOPLE THAT I JUST SAW
10 WHILE MAKING ROUNDS. AND I WAS THEIR ATTENDING
11 DOCTOR FOR SIX WEEKS. AND I DON'T GENERALLY KEEP
12 CLINICAL DATA ON SUCH PATIENTS EXCEPT FOR THE
13 LABORATORY RESULTS.
14 Q. HOW MANY OF THESE PATIENTS WERE SMOKERS, DO
15 YOU KNOW THAT?
16 A. I DON'T KNOW THAT. I DIDN'T TAKE THAT
17 INFORMATION DOWN AT THE TIME.
18 Q. NOW, DOCTOR, YOU SAID THAT STUDY WAS ONE OF
19 THE REASONS THAT YOU -- STRIKE THAT.
20 DID YOU TESTIFY EARLIER THAT UP UNTIL FOUR
21 YEARS AGO, YOU TESTED ALL THE PATIENTS YOU
22 ENCOUNTERED WITH SMALL CELL CANCER?
23 (OBJECTION) MR. NORTHRIP: OBJECTION TO THE
24 FORM.
25 THE WITNESS: NO.

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1 BY MS. WALTERS:

2 Q. DID YOU NOT SAY THAT?

3 A. NO.

4 Q. WHAT WAS YOUR PRACTICE UP UNTIL FOUR YEARS

5 AGO WITH RESPECT TO THE SMALL CELL CANCER PATIENTS

6 OF THE LUNG THAT YOU ENCOUNTERED?

7 MR. NORTHRIP: ARE YOU ASKING HIM AS

8 TO DURHAM MEDICAL CENTER OR THE VETERANS MEDICAL

9 CENTER OR ARE YOU ASKING HIM BOTH EXPERIENCES?

10 MS. WALTERS: BOTH.

11 THE WITNESS: WELL, AS I STATED

12 EARLIER, I ACTUALLY HAD DIFFERENT PROCEDURES

13 DEPENDING ON THE PATIENTS I SPECIFICALLY WOULD SEE

14 WITH THE QUESTION DID THEY HAVE SMALL CELL

15 CARCINOMA VERSUS CARCINOID, IN WHICH CASE IF I HAD

16 THE OPPORTUNITY, I WOULD ANALYZE THE URINE IN ALL

17 OF THESE PATIENTS THROUGHOUT THE YEARS VERY

18 CONSISTENTLY.

19 NOW, WHAT I'VE DONE IN MY ROLE AS AN

20 INTERNIST AT THE VETERANS ADMINISTRATION HOSPITAL

21 HAS VARIED FROM TIME TO TIME. AT THE TIME I WAS

22 DOING THAT STUDY, I WANTED TO SEE HOW OFTEN PEOPLE

23 WITH TUMORS MAY HAVE ALTERED SEROTONIN SO I DID

24 ALL THE PATIENTS I ENCOUNTERED CONSECUTIVELY.

25 BY MS. WALTERS:

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1 Q. BEFORE THAT TIME, BEFORE THE TIME OF THAT
2 STUDY WHICH WAS IN 1979, HOW OFTEN DID YOU TEST
3 PATIENTS THAT YOU ENCOUNTERED AT THE V.A. FOR
4 SEROTONIN?
5 A. FROM TIME TO TIME, I WOULD TEST THEM BUT
6 THERE WAS NO PATTERN AND IT WAS CERTAINLY THE
7 MAJORITY OF THEM I DIDN'T TEST. IN OTHER WORDS,
8 IT WOULD BE AN OCCASIONAL PATIENT I MIGHT TEST,
9 BUT MOST OF THE TIME I DIDN'T.
10 Q. AND YOU ONLY TESTED THEM FOR URINE?
11 A. SOMETIMES I MIGHT HAVE TESTED THEM ALSO FOR
12 SERUM SEROTONIN AND, AGAIN, IN A TOTALLY SORT OF
13 HAPHAZARD AT RANDOM MANNER, I MEAN --
14 Q. DID YOU EVER ANALYZE THE RESULTS OF ANY OF
15 THIS TESTING?
16 A. WELL, WHEN I WOULD TEST THE PERSON OVER THE
17 YEARS, I WOULD ANALYZE THE RESULTS. AGAIN, I
18 WOULD ANALYZE THE SAMPLE, BUT IF YOU'RE NOT DOING
19 IT IN A CONSECUTIVE MANNER, THEN IT'S A LITTLE
20 HARD TO GET A FIRM INTERPRETATION. BUT OVER THE
21 YEARS, I'VE PROBABLY ANALYZED, YOU KNOW, I'D
22 ESTIMATE MAYBE, I DON'T KNOW, MAYBE A HUNDRED
23 PATIENTS OVER MANY YEARS, OVER THE 17 YEARS OR SO.
24 Q. I'M TALKING ABOUT BEFORE FOUR YEARS AGO, CAN
25 YOU GIVE ME A NUMBER FOR HOW MANY YOU TESTED UP TO

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1 THAT POINT?

2 A. I ACTUALLY COULDN'T GIVE YOU A NUMBER UP

3 UNTIL THAT POINT. I COULDN'T DO THAT.

4 Q. AND AS YOU THINK BACK NOW, CAN YOU RECALL

5 WHETHER THERE WERE ANY ELEVATED SEROTONIN URINE

6 SAMPLES IN ANY OF THESE SMALL CELL CANCER

7 PATIENTS?

8 A. THE THING I'VE DONE MOST CONSISTENTLY IS

9 I'VE ANALYZED FOR 17 YEARS, WHEN I DID ANALYZE IT,

10 THE 5-HIAA. I'VE DONE THAT OVER THE ENTIRE PERIOD

11 OF TIME. THE SEROTONIN I DID USING A METHOD FOR A

12 NUMBER OF YEARS AND THEN I WOULD, FOR REASONS OF

13 DECREASED TECHNICAL SUPPORT IN THE LAB, I STOPPED

14 IT FOR A NUMBER OF YEARS, DEVELOPED A NEW METHOD

15 AND THEN RESUMED IT. SO I CAN'T SAY THAT I'VE

16 TESTED THEM ALL FOR SEROTONIN OVER THE YEARS.

17 I'VE TESTED -- THE ONES I HAVE TESTED, IF I'VE

18 TESTED THEM, IT'S BEEN THE MINIMUM THING I WOULD

19 HAVE DONE IS THE 5-HIAA BECAUSE THAT HAS BEEN

20 AVAILABLE IN MY LABORATORY SINCE '70. AND SO --

21 Q. DO YOU RECALL, AND AGAIN LIMITING OURSELVES

22 TO THOSE SMALL CELL CANCER PATIENTS THAT YOU DID

23 HAPHAZARDLY OR RANDOMLY TEST PRIOR TO FOUR YEARS

24 AGO FOR 5-HIAA, WHETHER ANY OF THEM HAD ELEVATED

25 READINGS?

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1 A. SEARCHING MY MEMORY, I CAN RECALL -- AGAIN,
2 I DON'T HAVE THIS IN ANY SORT OF A COMPUTERIZED
3 FORM -- I CAN RECALL ONLY SIX PATIENTS OVER THE
4 YEARS THAT HAD 5-HIAA OR SEROTONIN ELEVATED THAT
5 HAD OAT CELL CARCINOMAS.
6 Q. I'M TALKING UP UNTIL FOUR YEARS AGO.
7 A. LET'S SEE. WHY ARE WE CONCENTRATING ON FOUR
8 YEARS? THIS STUDY WAS DONE --
9 Q. THAT'S THE TIME PERIOD YOU USED FOR WHEN YOU
10 DID THE TEST.
11 (OBJECTION) MR. SIRRIDGE: I'M GOING TO OBJECT TO
12 THAT. I'M NOT SO SURE THERE'S ANY UNDERSTANDING
13 BY ANYONE HERE ABOUT THE FOUR-YEAR PERIOD BEING
14 TIED TO WHEN HE STARTED DOING CERTAIN TESTS.
15 BY MS. WALTERS:
16 Q. IS THERE A PERIOD IN TIME WHEN YOU CHANGED
17 YOUR PROCEDURE? I THOUGHT YOU USED THE TIME FRAME
18 OF FOUR YEARS AGO.
19 A. WELL, I BELIEVE SHE CAN READ ME BACK WHAT I
20 SAID, BUT I BELIEVE THAT I WAS SAYING THAT THIS --
21 LET'S SEE -- THIS PARTICULAR STUDY THAT WAS UNDER
22 DISCUSSION WAS PUBLISHED IN 1979 AND I ESTIMATED
23 THAT I DID COLLECT THE DATA IN LATE '78 AND EARLY
24 '79 PROBABLY BECAUSE OF THE LAGS IN PUBLICATION.
25 SO THAT WOULD HAVE PUT US BACK SEVEN-AND-A-HALF

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1 YEARS AGO RATHER THAN FOUR YEARS AGO. I'M NOT
2 SURE WHERE THE FOUR ENTERED THE DISCUSSION.
3 Q. DID YOU CHANGE YOUR PROCEDURES AS A RESULT
4 OF THE 1979 STUDY?
5 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
6 THE WITNESS: WHAT KIND OF PROCEDURES
7 DO YOU MEAN? DO YOU MEAN PROCEDURES OF TESTING
8 PATIENTS?
9 BY MS. WALTERS:
10 Q. THE PROCEDURE THAT YOU HAD OF RANDOMLY OR
11 HAPHAZARDLY TESTING SMALL CELL CANCER PATIENTS FOR
12 THE URINARY 5-HIAA.
13 (OBJECTION) MR. SIRRIDGE: I'M GOING TO OBJECT TO
14 THE FORM OF RANDOMLY AND HAPHAZARDLY BEING USED
15 SYNONYMOUSLY.
16 MS. WALTERS: I WAS USING THE
17 DOCTOR'S TERMS.
18 MR. SIRRIDGE: I'M NOT SO SURE HE
19 USED THEM SYNONYMOUSLY.
20 THE WITNESS: WHEN I SAID RANDOMLY,
21 THAT MEANS I DIDN'T DO THEM WITH ANY PATTERN. I
22 DIDN'T DO THEM WITH ANY SPECIFIC STUDY IN MIND. I
23 WOULD SAY THAT THE WAY I DID THEM BEFORE THE
24 STUDY, THIS STUDY OF 1979, AND THE WAY I DO THEM
25 SINCE THE STUDY OF 1979 HAS BEEN ABOUT THE SAME

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1 WHEN IT'S PATIENTS THAT ARE NOT UNDER ACTIVE
2 CONSIDERATION FOR WHETHER THEY HAVE A CARCINOID OR
3 OAT CELL. NOW, THOSE PATIENTS, I HAVE ALWAYS DONE
4 ALL OF THEM THAT I'M CALLED ON TO SEE THAT I CAN
5 OBTAIN A 24-HOUR URINE.
6 BY MS. WALTERS:
7 Q. ALL SMALL CELL CANCER OF THE LUNG PATIENTS?
8 (OBJECTION) MR. NORTHRIP: OBJECT TO THE FORM. I
9 THINK IT MISSTATES HIS TESTIMONY. I THINK IT
10 MISSTATES HIS TESTIMONY.
11 THE WITNESS: YES, I THINK IT DOES.
12 MS. WALTERS: COULD YOU READ BACK HIS
13 PRIOR ANSWER?
14 (DESIGNATED QUESTIONS AND ANSWERS ARE
15 READ)
16 BY MS. WALTERS:
17 Q. SO, DOCTOR, YOUR PRACTICE WITH RESPECT TO
18 SMALL CELL CANCER PATIENTS OF THE LUNG HAS NOT
19 CHANGED AS A RESULT OF THE 1979 STUDY; IS THAT
20 CORRECT?
21 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM OF
22 THE QUESTION.
23 THE WITNESS: PRACTICE?
24 BY MS. WALTERS:
25 Q. TESTING PRACTICE AND PROCEDURES.

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1 MR. SIRRIDGE: AND I'LL ALSO ADD IT'S
2 BEEN ASKED AND ANSWERED ABOUT TWO MINUTES AGO.
3 THE WITNESS: COULD YOU READ ME MY
4 ANSWER?
5 MS. WALTERS: I DON'T REMEMBER ASKING
6 THE QUESTION. YOU CAN ANSWER IT AGAIN.
7 MR. SIRRIDGE: IF YOU CAN UNDERSTAND
8 THE QUESTION --
9 THE WITNESS: I'M NOT SURE --
10 MR. NORTHRIP: WHY DON'T YOU READ THE
11 QUESTION BACK?
12 BY MS. WALTERS:
13 Q. DOCTOR, DID YOUR PRACTICES AND PROCEDURES
14 WITH RESPECT TO TESTING LUNG CANCER PATIENTS,
15 SMALL CELL LUNG CANCER PATIENTS FOR URINE 5-HIAA
16 CHANGE AS A RESULT OF YOUR 1979 STUDY?
17 A. I WOULD SAY IT HASN'T CHANGED AS A RESULT OF
18 MY STUDY.
19 Q. IS THIS THE ONLY STUDY THAT YOU'VE CONDUCTED
20 REGARDING SEROTONIN LEVELS IN SMALL CELL CANCER
21 PATIENTS WHERE THE CANCER IS IN THE LUNG?
22 A. WELL, IT'S THE ONLY STUDY THAT I
23 SPECIFICALLY WAS LOOKING AT SEROTONIN IN CANCER
24 PATIENTS. AT OTHER TIMES, I HAVE STUDIED CANCER
25 PATIENTS WITH TUMORS OF THE LUNG WHEN I'M

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1 EVALUATING A NEW ANALYTICAL PROCEDURE FOR THE
2 DIAGNOSIS OF CARCINOID TUMORS. AND, FREQUENTLY, I
3 WILL TRY AND OBTAIN BLOOD OR URINE ON A GROUP OF
4 PATIENTS WHO HAVE TUMORS THAT AREN'T THOUGHT TO BE
5 CARCINOID TUMORS TO SEE WHAT THEIR LEVELS OF THESE
6 THINGS ARE. SO THEY MIGHT BE INCLUDED IN OTHER
7 STUDIES.
8 Q. SMALL CELL CANCER PATIENTS MIGHT BE INCLUDED
9 IN OTHER STUDIES?
10 A. THEY MIGHT BE INCLUDED AMONGST THE GROUP OF
11 PATIENTS WITH OTHER CANCERS, NOT SPECIFICALLY
12 SEEKING OUT LUNG CANCER PATIENTS, BUT IF ONE IS
13 LOOKING AT ALL SORTS OF NON-CARCINOID CANCER
14 PATIENTS, THEY MIGHT BE INCLUDED.
15 Q. HAVE YOU EVER HAD ANY -- HAVE YOU EVER DONE
16 ANY OTHER RESEARCH OR STUDY THAT SPECIFICALLY
17 BROKE DOWN SMALL CELL LUNG CANCER PATIENTS AND
18 EXAMINED THE SEROTONION AND THEIR 5-HIAA LEVEL OF
19 THOSE?
20 A. SPECIFICALLY BROKE IT DOWN? WELL, SEE,
21 SOMETIMES THE PATIENTS COULD BE INCLUDED IN THE
22 STUDY.
23 Q. I REALIZE THAT, BUT I'M ASKING YOU WHETHER
24 IN ANY OF THE STUDIES YOU EVER BROKE IT DOWN?
25 A. YOU MEAN TO SAY WERE THERE SUCH PATIENTS

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1 WITH THIS DIAGNOSIS IN THE STUDY?

2 Q. AND WAS THE STUDY BROKEN DOWN IN SUCH A WAY

3 THAT YOU COULD CORRELATE THE READING WITH THE

4 TUMOR TYPE?

5 A. TO SOME EXTENT, YES, ALTHOUGH IT MAY NOT

6 HAVE BEEN COMPREHENSIVE. TO SOME EXTENT, THERE

7 WAS SOME STUDIES WHERE ONE COULD CORRELATE IT.

8 Q. WHICH STUDIES ARE THOSE?

9 A. WELL, THERE'S TWO STUDIES. THE MOST RECENT

10 STUDY WAS A STUDY ON HOW OFTEN SEROTONIN AND

11 CERTAIN OTHER PEPTIDE HORMONES WERE ELEVATED IN A

12 PATIENT WITH CARCINOID TUMORS AND WHETHER THESE

13 MATERIALS PLAYED A CHANGE IN RELATIONSHIP TO WHEN

14 THE PATIENT'S FLUSHED, HAD FLUSHING. THERE WAS A

15 STUDY.

16 Q. WHAT STUDY WAS THAT, DO YOU RECALL THE YEAR?

17 A. THAT STUDY WOULD HAVE BEEN ON MY CURRICULUM

18 VITAE, RIGHT? THAT STUDY WAS STUDY 171, THE ROLE

19 OF NEUROPEPTIDES AND SEROTONIN IN THE DIAGNOSIS OF

20 CARCINOID TUMORS, AMERICAN JOURNAL OF MEDICINE,

21 '81.

22 Q. ANY OTHERS?

23 A. ANOTHER STUDY WOULD HAVE BEEN IN CLINICAL

24 CHEMISTRY. THAT WAS STUDY NUMBER 169. FELDMAN,

25 J.M., URINARY SEROTONIN IN THE DIAGNOSIS OF

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1 CARCINOID TUMORS, CLINICAL CHEMISTRY, VOLUME 32,
2 PAGE 840, 1986. THOSE ARE THE ONLY TWO OTHER
3 STUDIES THAT I CAN RECALL WHERE THERE WAS
4 SEROTONIN WHERE IT WAS BROKEN DOWN.
5 Q. SEROTONIN AND 5-HIAA?
6 A. SEROTONIN AND 5-HIAA.
7 Q. NOW, DO YOU HAVE A COPY OF THAT ARTICLE
8 NUMBER 172 HERE? BECAUSE THAT SAYS "IN PRESS" ON
9 IT, ON THIS CURRICULUM VITAE.
10 A. IT WAS PUBLISHED SUBSEQUENT TO THE
11 CURRICULUM VITAE. I DON'T THINK -- I DON'T HAVE
12 ONE HERE.
13 MR. SIRRIDGE: I DON'T THINK SO.
14 BY MS. WALTERS:
15 Q. DO YOU RECALL HOW MANY SMALL CELL CANCERS OF
16 THE LUNG WERE EXAMINED IN THAT CASE AND THE
17 CONTEXT IN WHICH THEY WERE EXAMINED?
18 (OBJECTION) MR. NORTHRIP: OBJECT TO THE FORM.
19 MR. SIRRIDGE: WOULD YOU READ THE
20 QUESTION BACK, COULD YOU, PLEASE?
21 (DESIGNATED QUESTION IS READ)
22 THE WITNESS: WELL, I DON'T HAVE THAT
23 REPORT HERE WITH ME SO I DON'T KNOW THE TOTAL
24 NUMBER OF TUMOR PATIENTS OR THE TOTAL NUMBER OF
25 CARCINOID PATIENTS OR NON-TUMOR PATIENTS THAT WERE

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1 EXAMINED. MY NOTES INDICATE THAT THERE WERE FOUR
2 PATIENTS WITH SMALL CELL CARCINOMA IN THAT. I
3 CAN'T REFER TO THE ACTUAL ARTICLE AT THE MOMENT.
4 BY MS. WALTERS:
5 Q. WOULD THOSE FOUR PATIENTS BE SMALL CELL
6 CANCER OF THE LUNG?
7 A. MY NOTES INDICATE THAT THOSE FOUR PATIENTS
8 WERE SMALL CELL CARCINOMA OF THE LUNG.
9 Q. AND WHAT WERE THEY TESTED FOR?
10 A. THEY WERE TESTED FOR 5-HIAA, AND I'M NOT
11 SURE IF THEY WERE ALL TESTED FOR SEROTONIN OR
12 NOT. I'M NOT SURE ABOUT THAT. THEY ALSO WERE
13 TESTED FOR -- I'M NOT SURE WITHOUT REFERRING TO
14 THE PAPER, WITHOUT GETTING THE PAPER. IN THE
15 PAPER, THEY WERE PROBABLY ALSO TESTED FOR
16 SUBSTANCE P, I WOULD THINK, BECAUSE THE PAPER
17 DEALT WITH THAT.
18 Q. WHEN YOU SAY THEY WERE PROBABLY TESTED FOR
19 SEROTONIN, DO YOU MEAN BOTH BLOOD AND URINE OR ONE
20 OR THE OTHER?
21 A. IT COULD BE BOTH BLOOD AND URINE. MY
22 RECOLLECTION IS THAT PATIENTS IN THAT PAPER WERE
23 -- SOME WERE TESTED FOR BOTH BLOOD AND URINE, BUT
24 I CAN'T BE CERTAIN WITHOUT LOOKING AT THE PAPER TO
25 SEE WHAT I WROTE.

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1 Q. DO YOU RECALL WHAT THE RESULTS ARE, WHETHER
2 THERE WAS ANY EVIDENCE OF SEROTONIN OR 5-HIAA
3 ELEVATION IN ANY OF THESE FOUR?
4 A. MY NOTES INDICATE THAT THESE FOUR DID NOT
5 HAVE ELEVATION OF 5-HIAA. AND IF THEY WERE -- IF
6 TESTED, I'D HAVE TO SEE HOW MANY OF THE FOUR WERE
7 TESTED, IT MIGHT HAVE BEEN ALL, THAT THEY DIDN'T
8 HAVE ELEVATION OF SEROTONIN, EITHER.
9 Q. WHAT NOTES ARE YOU REFERRING TO?
10 A. I'M REFERRING TO THE NOTES HERE
11 (INDICATING).
12 Q. YOU HAVE A YELLOW PAD IN FRONT OF YOU THAT
13 CONTAINS YOUR HANDWRITTEN NOTES?
14 MR. NORTHRIP: IS THAT A QUESTION?
15 THE WITNESS: YES, A YELLOW PAD THAT
16 CONTAINS MY HANDWRITTEN NOTES.
17 MS. WALTERS: WHY DON'T WE MARK THAT
18 WHOLE PAD AS P-FELDMAN-1 FOR IDENTIFICATION.
19 (EXHIBITS P-FELDMAN-1A THROUGH
20 P-FELDMAN-1X, HANDWRITTEN NOTES, ARE MARKED FOR
21 IDENTIFICATION)
22 BY MS. WALTERS:
23 Q. DOCTOR, THE OTHER ARTICLE THAT YOU'VE
24 REFERRED TO IS NUMBER 169 ON YOUR CURRICULUM
25 VITAE, AND THAT'S AN ARTICLE THAT WAS PUBLISHED IN

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1986 IN CLINICAL CHEMISTRY; IS THAT CORRECT?

A. THAT'S CORRECT.

Q. HOW MANY SMALL CELL CANCERS OF THE LUNG WERE EXAMINED THERE?

A. AGAIN, I DON'T HAVE THE ARTICLE PRESENT IN THE ROOM WHERE WE'RE TAKING THE DEPOSITION, BUT MY NOTES INDICATE THAT 11 PATIENTS WERE EXAMINED IN THAT PAPER THAT HAD SMALL CELL CARCINOMA OF THE LUNG.

Q. AND HOW MANY OF THE 11 HAD ELEVATED LEVELS OF SEROTONIN?

A. MY NOTES INDICATE THAT FIVE OF THE ELEVEN HAD -- NO. I'D LIKE TO REPHRASE THAT. DO YOU HAVE THAT ONE?

MR. SIRRIDGE: I THINK WE HAVE THAT ONE.

(BRIEF RECESS)

MS. WALTERS: PLEASE MARK THIS AS P-FELDMAN-2.

(EXHIBIT P-FELDMAN-2, CURRENT CURRICULUM VITAE, IS MARKED FOR IDENTIFICATION)

MS. WALTERS: THIS IS OFF THE RECORD.

(OFF-THE-RECORD DISCUSSION)

MS. WALTERS: WHAT WAS THE LAST QUESTION?

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1 (DESIGNATED QUESTION AND ANSWER ARE
2 READ)
3 BY MS. WALTERS:
4 Q. HOW MANY OF THE 11 SMALL CELL CANCERS OF THE
5 LUNG HAD ELEVATED SEROTONIN OR 5-HIAA LEVELS?
6 A. CAN I READ THE PARAGRAPH THAT'S RELEVANT TO
7 THAT OR SHOULD I --
8 Q. WHATEVER IS EASIER FOR YOU.
9 A. SHOULD I JUST PARAPHRASE IT?
10 Q. I PREFER THAT YOU PARAPHRASE IT, BUT GO
11 AHEAD.
12 MR. SIRRIDGE: IF YOU NEED TO READ
13 THE PARAGRAPH, GO AHEAD, AND THEN ANSWER THE
14 QUESTION.
15 BY MS. WALTERS:
16 Q. JUST TELL US WHAT PAGE YOU'RE ON.
17 A. IT'S ON PAGE 842, THE FIRST COMPLETE
18 PARAGRAPH ON THE PAGE: ONLY TWO OF THE 50
19 PATIENTS WITH SOLID NON-CARCINOID TUMORS HAD AN
20 ABOVE-NORMAL URINARY EXCRETION OF SEROTONIN. ONE
21 PATIENT WITH A SMALL-CELL ("OAT CELL") CARCINOMA
22 OF THE LUNG HAD A SEROTONIN EXCRETION OF ONE POINT
23 NINE MICRO/MOLES PER 24 HOURS; THE OTHER PATIENT
24 WITH AN INTERMEDIATE-CELL CARCINOMA OF THE LUNG
25 HAD A SEROTONIN EXCRETION OF 13 POINT THREE

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1 MICRO/MOLES PER 24 HOURS. THREE PATIENTS WITH
2 SMALL-CELL CARCINOMA OF THE LUNG HAD SLIGHTLY
3 INCREASED URINARY EXCRETION OF 5-HIAA AND NORMAL
4 SEROTONIN EXCRETION. THE REMAINING SIX PATIENTS
5 WITH SMALL-CELL CARCINOMA OF THE LUNG HAD NORMAL
6 EXCRETION OF SEROTONIN AND 5-HIAA. NONE OF THE 55
7 PATIENTS EVALUATED FOR FLUSHING OR DIARRHEA, WHO
8 DID NOT HAVE CARCINOID TUMORS, HAD AN ABOVE-NORMAL
9 URINARY EXCRETION OF EITHER SEROTONIN OR 5-HIAA.
10 SO THE ESSENCE, TO READ THE PARAGRAPH AND TO
11 ANSWER THE QUESTION, I'D LIKE TO INDICATE THAT
12 WHAT I'M DOING NOW IS I'M LOOKING AT THE RECORDS
13 TO GET A FEELING BECAUSE THIS JOURNAL REQUIRED
14 THAT THE EXCRETION BE PUT IN MICRO/MOLES AND I'M
15 USED TO DEALING WITH MILLIGRAMS, AND I'M JUST
16 TRYING TO GET A FEELING FOR THE MAGNITUDE OF THOSE
17 NUMBERS BECAUSE IN MY DAY-TO-DAY WORK, I DON'T USE
18 MICRO/MOLES.
19 BUT TO ANSWER THE QUESTION, ONE PATIENT, IN
20 MY OWN WORDS, ONE PATIENT HAD A MINIMALLY-ELEVATED
21 EXCRETION OF SEROTONIN, ONE POINT NINE
22 MICRO/MOLES, WHERE THE UPPER RANGE OF NORMAL IS
23 ONE POINT 33. THE OTHER PATIENT WHO HAD HAD AN
24 INTERMEDIATE-CELL CARCINOMA OF THE LUNG HAD A
25 MODERATE EXCRETION OF SEROTONIN OF 13 POINT THREE

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1 MICRO/MOLES PER 24 HOURS. I DON'T GIVE IN THE
2 PAPER THE VALUES FOR 5-HIAA OR SAY WHAT THEY ARE
3 AND I CAN'T RECALL WHAT THEY WERE BECAUSE THE MAIN
4 THRUST OF THIS PAPER WAS DEALING WITH CARCINOIDS
5 AND THE OTHER LUNG TUMOR PATIENTS WERE A SIDE
6 ISSUE.
7 I THEN MENTION THAT THREE OTHER PATIENTS
8 WITH SMALL-CELL CARCINOMA HAD A SLIGHTLY INCREASED
9 URINARY EXCRETION OF 5-HIAA AND NORMAL SEROTONIN.
10 THE MAIN THRUST OF THIS PAPER WAS THE ROLE OF
11 URINARY SEROTONIN AND THE DIAGNOSIS OF CARCINOMA
12 TUMORS, NOT THE ROLE OF 5-HIAA. SO THAT'S WHY I
13 DON'T HAVE ALL OF 5-HIAA GIVEN IN THE PAPER. MY
14 RECOLLECTION OF THE THREE PATIENTS THAT I SAID HAD
15 A SLIGHTLY ELEVATED WAS THAT THEIR VALUES WERE
16 BETWEEN EIGHT AND TEN IS WHAT I USUALLY CALL
17 SLIGHTLY ELEVATED.
18 Q. EIGHT AND TEN WHAT?
19 A. EIGHT AND TEN MILLIGRAMS PER 24 HOURS. MOST
20 OF THE DEPOSITIONS HAVE BEEN GIVEN IN MILLIGRAMS
21 PER 24 HOURS, I PRESUME; IS THAT RIGHT?
22 Q. I THINK WE BETTER CLARIFY IT AS WE'VE GONE
23 ALONG.
24 A. SO FAR IT'S ALL BEEN, EXCEPT FOR THIS PAPER,
25 BECAUSE SOME OF THE JOURNALS REQUIRE THE

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1 INTERNATIONAL SYSTEM OF UNITS FOR PUBLICATION.

2 Q. SO, DOCTOR, AS I UNDERSTAND IT THEN, OF THE

3 11 SMALL CELL CANCER PATIENTS, FIVE OF THEM HAD

4 EITHER INCREASED URINARY EXCRETION OF SEROTONIN OR

5 URINARY EXCRETION OF 5-HIAA?

6 A. YES, EXCEPT THAT THREE OF THEM HAD ONLY A

7 VERY MINIMAL ELEVATION OF URINARY EXCRETION OF

8 5-HIAA. IN FACT, THE AMOUNT OF ELEVATION THEY HAD

9 IN MY LABORATORY IS SLIGHTLY ABOVE NORMAL. AND IN

10 SOME LABORATORIES, IT ACTUALLY WOULD BE WITHIN

11 THEIR NORMAL RANGE.

12 Q. AND THERE WAS NO TESTING FOR BLOOD

13 SEROTONIN; IS THAT CORRECT?

14 A. THERE WAS NO TESTING IN THIS PAPER FOR BLOOD

15 SEROTONIN IN THE PATIENTS THAT DIDN'T HAVE THE

16 CARCINOID BECAUSE THE MAIN THRUST OF THE PAPER WAS

17 CARCINOIDS.

18 Q. WERE CARCINOIDS TESTED FOR --

19 MR. NORTHRIP: I DON'T BELIEVE THE

20 DOCTOR HAS COMPLETED HIS ANSWER, HAS HE?

21 THE WITNESS: IN THIS PARTICULAR

22 PAPER, MANY OF THE CARCINOID PATIENTS WERE TESTED

23 FOR PLATELET SEROTONIN CONCENTRATION WHICH IS ONE

24 OF THE THREE WAYS IN WHICH ONE CAN ASSESS BLOOD

25 SEROTONIN.

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1 BY MS. WALTERS:

2 Q. IS THERE ANY REASON WHY THE SMALL CELL

3 CANCER PATIENTS WERE NOT TESTED FOR PLATELET SERUM

4 CONCENTRATION?

5 A. WELL, I DON'T KNOW, IN FACT, IF THEY WEREN'T

6 TESTED OR WERE TESTED BECAUSE THE DATA AS I GAVE

7 ON THIS PAPER WAS MAINLY THE URINARY SEROTONIN

8 5-HIAA BECAUSE THE SMALL-CELL CARCINOMA PATIENTS

9 WERE INCIDENTAL TO THE STUDY BECAUSE THE TITLE OF

10 THE STUDY WAS URINARY SEROTONIN IN THE DIAGNOSIS

11 OF CARCINOID TUMORS AND I WAS REALLY LOOKING AT

12 THE IMPORTANCE OF THE URINARY SEROTONIN IN THIS

13 PARTICULAR STUDY. USUALLY, ONE HAS TO RESTRICT

14 WHAT THEY DO TO A CERTAIN QUESTION THEY'RE TRYING

15 TO ANSWER. AND THIS PARTICULAR PAPER, I WAS -- MY

16 QUESTION WAS IS URINARY SEROTONIN MEASUREMENTS

17 HELPFUL IN THE DIAGNOSIS OF CARCINOID TUMORS. I

18 WASN'T REALLY LOOKING AT PLATELET SEROTONIN.

19 Q. DID YOU FIND THAT URINE SEROTONIN IS HELPFUL

20 IN THE DIAGNOSIS OF CARCINOID TUMORS?

21 A. YES, I DID. I FOUND IT WAS HELPFUL.

22 Q. ARE THERE ANY OTHER STUDIES THAT YOU'VE DONE

23 OR RESEARCH THAT YOU'VE BEEN INVOLVED WITH THAT

24 EXAMINE SMALL CELL CANCER OF THE LUNG?

25 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.

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1 THE WITNESS: I CAN'T RECALL -- WOULD
2 YOU REPHRASE THE QUESTION, OTHER STUDIES?
3 BY MS. WALTERS:
4 Q. ANY OTHER STUDIES -- WERE THERE ANY OTHER
5 STUDIES OR RESEARCH THAT YOU HAVE BEEN INVOLVED IN
6 IN SMALL CELL CANCER OF THE LUNG?
7 MR. NORTHRIP: YOU MEAN IN ADDITION
8 TO WHAT HE'S ALREADY TOLD YOU ABOUT?
9 MS. WALTERS: CORRECT.
10 THE WITNESS: I CAN'T RECALL ANY
11 OTHER STUDIES.
12 BY MS. WALTERS:
13 Q. LOOKING BACK AT THIS 1986 ARTICLE THAT WE'VE
14 BEEN DISCUSSING FROM CLINICAL CHEMISTRY, WHAT
15 PERCENTAGE OF THE CARCINOIDS WERE CARCINOIDS OF
16 THE BRONCHUS?
17 A. THE BEST WAY TO PROBABLY LOOK AT THAT IS IN
18 FIGURE ONE ON PAGE 841, WHERE I SHOW THE FIGURE
19 HAVING DOTS, EACH REPRESENTING ONE PATIENT WITH A
20 CARCINOID OF THE BRONCHUS.
21 Q. HOW MANY DOTS ARE THERE?
22 A. IT APPEARS THAT THERE ARE EIGHT DOTS.
23 THERE'S SORT OF A XEROX SMUDGE, WHICH I DON'T
24 THINK IS A POINT BUT I CAN'T BE SURE WITHOUT
25 LOOKING AT AN ORIGINAL COPY. THERE'S A LITTLE

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1 SMUDGE IN THE COLUMN WHERE IT SAYS BRONCHUS.
2 Q. AND FIGURE ONE SHOWS URINARY EXCRETION OF
3 SEROTONIN?
4 A. THAT'S CORRECT.
5 Q. AND HOW MANY OF THE CARCINOIDS OF THE
6 BRONCHUS HAD NORMAL SEROTONIN LEVELS?
7 A. ONLY ONE PATIENT WAS NOT -- DID NOT HAVE AN
8 ELEVATED LEVEL AS LOOKING AT THIS FIGURE. HE WAS
9 AT THE LOWER LIMITS OF THE NORMAL LEVEL.
10 Q. HOW MANY WERE SLIGHTLY ELEVATED?
11 A. I WOULD CONSIDER THE FOUR THAT WERE UNDER --
12 WELL, I WOULD CONSIDER -- I WOULD CONSIDER IF THE
13 VALUE IS DOUBLED, IT'S MORE THAN SLIGHTLY ELEVATED
14 SO I WOULD SAY THAT ONE PATIENT WAS SLIGHTLY
15 ELEVATED, ONE PATIENT OF THE BRONCHIAL CARCINOIDS
16 WAS SLIGHTLY ELEVATED.
17 Q. HOW MANY OF THEM WOULD YOU CALL HIGHLY
18 ELEVATED?
19 A. I WOULD CALL THE TOP TWO HIGHLY ELEVATED.
20 Q. AND WHAT WOULD YOU CALL THE REST?
21 A. I WOULD CALL THE MIDDLE FOUR MODERATELY
22 ELEVATED. AGAIN, THIS IS USING THE TERMS IN A
23 SOMEWHAT LOOSE MANNER BECAUSE ONE COULD DEFINE IT
24 DIFFERENT WAYS.
25 Q. TELL ME --

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1 A. CLEARLY BUT MODERATELY.

2 Q. I'M SORRY. TELL ME OF THE -- AND WHAT WERE

3 THE RANGES OF THE ONES THAT WERE CLEARLY BUT

4 MODERATELY, WHAT WAS THE LOW RANGE?

5 A. THEY RANGED -- I'D HAVE TO TRY AND

6 INTERPOLATE FROM THE THING, IT LOOKS LIKE THE

7 LOWEST ONE WOULD BE RANGING FROM ABOUT THREE AND

8 THE HIGHEST WOULD BE PERHAPS SEVEN-AND-A-HALF, THE

9 NORMAL RANGE BEING POINT THREE TO ONE POINT THREE,

10 BUT WE'RE NOW TALKING ABOUT MICRO/MOLES FOR 24

11 HOURS, WHICH IS THE UNITS WHICH THIS PARTICULAR

12 PAPER IS IN.

13 Q. DOCTOR, WERE THESE PATIENTS THAT WERE ALL

14 EXAMINED IN THIS 1986 ARTICLE ALL PATIENTS THAT

15 YOU SAW ON CONSULTATION AT DUKE MEDICAL CENTER?

16 A. I HAVE TO DO THIS FROM MY RECOLLECTION. MY

17 RECOLLECTION IS THAT ALL THE PATIENTS THAT HAD

18 CARCINOID TUMORS WERE PATIENTS I WAS EITHER THE

19 PRIMARY PHYSICIAN FOR OR SAW IN CONSULTATION. I

20 CAN'T BE CERTAIN THAT THE PATIENTS -- AND, ALSO, I

21 CAN SAY THE SAME THING PROBABLY FOR THE PATIENTS

22 WITH THE FLUSHING. BUT I CAN'T BE CERTAIN ABOUT

23 THE PATIENTS WITH THE OTHER TUMORS, ALTHOUGH IT'S

24 LIKELY THAT I DID SEE THEM IN CONSULTATION.

25 AGAIN, THIS WAS PUBLISHED IN '86 AND WAS PROBABLY

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1 DONE, YOU KNOW, MAYBE '83, '84 TO '86. LET'S
2 SEE. MAYBE I STATE IT HERE. I THINK IT'S LIKELY
3 I PROBABLY SAW THEM IN CONSULTATION BUT I CAN'T
4 SAY WITH ABSOLUTE CERTAINTY. I JUST DESCRIBED
5 THEM AS BEING PATIENTS AND DIVIDED THEM INTO FOUR
6 GROUPS.
7 Q. DOCTOR, WHEN YOU REFER TO CARCINOID
8 PATIENTS, ARE YOU REFERRING TO PATIENTS THAT HAVE
9 BOTH BENIGN AND MALIGNANT LESIONS?
10 A. WELL, MY OWN CONCEPTION OF CARCINOID TUMORS
11 IS THAT THEY ARE ALL POTENTIALLY MALIGNANT
12 LESIONS. SOME HAVE A VERY LOW, LOW INCIDENCE OF
13 BEING MALIGNANT BUT THEY'RE POTENTIALLY
14 MALIGNANT. ONE CANNOT ALWAYS TELL WHEN THEY FIRST
15 SEE THE PATIENT WITH ABSOLUTE CERTAINTY IF THE
16 CLINICAL COURSE WILL BE A CLINICAL COURSE OF
17 BENIGN OR MALIGNANT DISEASE.
18 Q. ARE THE MAJORITY OF CARCINOIDS THAT YOU SEE
19 BENIGN?
20 (OBJECTION) MR. NORTHRIP: OBJECT TO THE FORM OF
21 THE QUESTION. HE JUST SAID THEY'RE ALL
22 POTENTIALLY MALIGNANT.
23 THE WITNESS: ALL POTENTIALLY
24 MALIGNANT.
25 BY MS. WALTERS:

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1 Q. ARE THE MAJORITY OF THE ONES YOU SEE, IN
2 FACT, BENIGN?
3 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
4 HOW ARE WE DEFINING "BENIGN"?
5 BY MS. WALTERS:
6 Q. DOCTOR, DO YOU USE THE TERM "BENIGN
7 CARCINOID"?
8 A. I USE THE TERM "BENIGN", BUT I CAN ONLY USE
9 IT ABSOLUTELY IN RETROSPECT IF SOMETHING'S BEHAVED
10 IN A BENIGN MANNER AFTER BEING OBSERVED FOR A
11 PERIOD OF TIME.
12 Q. ARE THE MAJORITY OF THE TUMORS, THE
13 CARCINOID TUMORS THAT YOU HAVE SEEN IN RETROSPECT,
14 BENIGN?
15 A. OVERALL, TAKING CARCINOIDS FROM ALL AREAS, A
16 MAJORITY HAVE PROBABLY BEHAVED MORE IN A MALIGNANT
17 FASHION.
18 Q. IS YOUR EXPERIENCE YOU THINK CONSISTENT WITH
19 THE LITERATURE ON THE SUBJECT?
20 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
21 THE WITNESS: MY EXPERIENCE? MY
22 EXPERIENCE WOULD NOT -- IT DEPENDS WHERE THE
23 LITERATURE -- I DON'T KNOW. THE LITERATURE IS
24 SUCH A BROAD THING, IT DEPENDS HOW THE LITERATURE
25 WAS COLLECTED. I THINK THAT THERE ARE CERTAIN

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1 SELECTION FACTORS THAT MIGHT DETERMINE THE TYPE OF
2 PATIENTS I WOULD SEE OVER THE TYPE OF PATIENTS
3 ANOTHER PHYSICIAN WOULD SEE AND REPORT IN THE
4 LITERATURE.
5 BY MS. WALTERS:
6 Q. WHAT ARE THE SELECTION FACTORS?
7 A. WELL, THE PATIENTS THAT I WOULD SEE PROBABLY
8 WOULD TEND TO BE MORE PROBLEM CASES THAT MAY HAVE
9 A TENDENCY TO BEHAVE AND HAVE A MALIGNANT COURSE.
10 THE PATIENTS A THORACIC SURGEON MIGHT SEE WOULD
11 PROBABLY TURN OUT OVER THE LONG HAUL TO BEHAVE
12 CLINICALLY IN A MORE BENIGN MANNER BECAUSE THE
13 PATIENTS I SEE, I SEE SOMETIMES BECAUSE THEY'VE
14 REPRESENTED A PROBLEM TO THEIR LOCAL MEDICAL
15 CENTER, EITHER THE TUMOR HAS COME BACK OR HAS
16 SPREAD TO ANOTHER AREA AND SO FORTH. SO I CAN'T
17 SAY THAT MY EXPERIENCE WILL REFLECT THE GENERAL
18 EXPERIENCE NECESSARILY.
19 Q. HOW ABOUT WITH RESPECT TO CARCINOIDS OF THE
20 LUNG, DO YOU SEE RETROSPECTIVELY MORE BENIGN OR
21 MORE MALIGNANT CARCINOIDS OF THE LUNG?
22 A. WITHIN THE LIMITS THAT I HAVE FOLLOWED --
23 HAVE FOLLOW-UP INFORMATION, I SEE MORE BENIGN.
24 BUT I PROBABLY WOULD SEE MORE MALIGNANT ONCE AGAIN
25 THAN WOULD, SAY, A THORACIC SURGEON WHO TAKES

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1 PEOPLE SIMPLY BECAUSE THEY HAVE A LUNG NODULE. SO
2 IT TURNS OUT, IN FACT, I PROBABLY HAVE SEEN MORE
3 WITH A BENIGN COURSE, BUT THE PREPONDERANCE WOULD
4 NOT BE AS STRIKING AS THAT OF A THORACIC SURGEON
5 WOULD SEE.
6 Q. HOW MANY CARCINOIDS OF THE LUNG WOULD YOU
7 HAVE SEEN -- LET ME REPHRASE IT.
8 DO YOU KEEP TRACK OF THE CARCINOIDS OF THE
9 LUNG THAT YOU SEE?
10 A. YES, I DO.
11 Q. DO YOU KEEP A RUNNING TALLY OF THEM?
12 A. YES, I DO.
13 Q. WHEN DID YOU START THE TALLY?
14 A. I STARTED THE TALLY IN 1970.
15 Q. AND DO YOU KEEP A RUNNING TALLY OF THE
16 NUMBER OF SMALL CELL CANCERS OF THE LUNG THAT YOU
17 SEE?
18 A. NO, NOT A FORMAL RUNNING TALLY.
19 Q. HOW MANY CARCINOIDS OF THE LUNG HAVE YOU
20 SEEN SINCE 1970?
21 A. I HAVE TO REFER TO THIS DATA I HAVE HERE.
22 I'M REFERRING TO A COMPUTER PRINT-OUT. DOES SHE
23 HAVE THAT?
24 MS. WALTERS: YES.
25 THE WITNESS: WHICH I BELIEVE YOU

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1 HAVE.

2 MS. WALTERS: YES.

3 MR. NORTHRIP: OFF THE RECORD.

4 (OFF-THE-RECORD DISCUSSION)

5 THE WITNESS: I HAVE THE COMPUTER

6 PRINT-OUT. IT INDICATES THERE'S A TOTAL OF 51

7 PATIENTS, 32 ON ONE SHEET AND 19 ON ANOTHER SHEET,

8 WHOSE EVIDENCE INDICATE TO ME THAT THEY HAD

9 CARCINOIDS THAT ORIGINATED IN THE BRONCHUS.

10 BY MS. WALTERS:

11 Q. SO YOU'VE HAD 51 PATIENTS SINCE 1970 WITH A

12 PRIMARY CARCINOID OF THE LUNG?

13 A. YES, THAT I'M CONFIDENT AROSE IN THE LUNG.

14 Q. AND THERE ARE NO OTHERS THAT YOU DON'T HAVE

15 ON THIS TALLY -- STRIKE THAT.

16 ARE THERE ANY OTHERS THAT YOU HAVE NOT

17 PLACED ON THIS TALLY?

18 A. ON THIS TALLY, THERE ARE NO OTHERS I HAVEN'T

19 PLACED ON THE TALLY THAT I WAS CONFIDENT WERE

20 CARCINOID TUMORS THAT AROSE IN THE LUNG THAT I HAD

21 AN ADEQUATE AMOUNT OF INFORMATION TO BE CERTAIN

22 ABOUT THIS.

23 Q. NOW, AT THE TOP OF THE FIRST PAGE -- WHY

24 DON'T WE MARK THIS P-FELDMAN-3 FOR IDENTIFICATION?

25 (EXHIBIT P-FELDMAN-3, COMPUTER

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1 PRINT-OUT, IS MARKED FOR IDENTIFICATION)
2 BY MS. WALTERS:
3 Q. ON THE FIRST PAGE OF P-3 FOR IDENTIFICATION,
4 AT THE TOP, IT'S LABELED BENIGN BRONCHIAL
5 CARCINOIDS AND A HISTORY OF CIGARETTE SMOKING?
6 A. RIGHT.
7 Q. EXCEPT IT SAYS GIGARETTE SMOKING.
8 A. THAT'S A TYPOGRAPHICAL ERROR I WOULD LIKE TO
9 APOLOGIZE FOR. I JUST NOTICED THAT YESTERDAY
10 MYSELF.
11 Q. HOW DID YOU COME TO DETERMINE THAT THESE 32
12 CARCINOIDS WERE BENIGN?
13 A. WELL, WHAT BENIGN MEANS HERE, AND THIS IS A
14 COMPUTER PRINT-OUT, AND WHAT IT MEANS IS THESE ARE
15 BRONCHIAL, AND THERE'S ONLY A LIMITED AMOUNT OF
16 SPACE FOR TITLES ON THIS PARTICULAR PRINT-OUT, BUT
17 WHAT IT WOULD MEAN IN A MORE DETAILED WAY IS THESE
18 ARE BRONCHIAL CARCINOID PATIENTS WHO HAD A BENIGN
19 CLINICAL COURSE, THAT IS WHILE I WAS ABLE TO
20 OBTAIN DATA ON HOW THEY DID, THE TUMOR DID NOT ACT
21 IN A MALIGNANT FASHION, THAT IS TO SPREAD TO
22 ANOTHER AREA OF THEIR BODY CAUSING THEM TO HAVE
23 TUMOR IN OTHER AREAS OR FOR THE TUMOR TO RESULT IN
24 THEIR DEATH.
25 Q. AND THEN ON --

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1 A. SO I'M USING IT IN A CLINICAL SENSE, THE
2 WORD BENIGN.
3 Q. ON THE THIRD PAGE, THIS PRINT-OUT BEGINS
4 WITH THE TITLE MALIGNANT BRONCHIAL TUMORS AND A
5 HISTORY OF CIGARETTE SMOKING?
6 A. YES.
7 Q. AND HOW DID YOU COME TO THE DESIGNATION OF
8 THESE 19 TUMORS AS MALIGNANT BRONCHIAL TUMORS?
9 A. THESE WERE PATIENTS THAT HAD BRONCHIAL
10 CARCINOID TUMORS THAT BEHAVED IN A MALIGNANT
11 CLINICAL FASHION, THAT IS THE TUMORS RECURRED OR
12 THEY MIGHT HAVE BEEN DIFFUSELY PRESENT AT THE TIME
13 OF DIAGNOSIS AND THEY RESULTED IN THE DEATH OF 18
14 OF THE 19 PATIENTS, AND THE ONE PATIENT WHO'S AT
15 THE TOP OF THE LIST WHO HASN'T DIED, THE TUMOR HAS
16 METASTASIZED TO BONE, LIVER, ET CETERA, AND SHOWED
17 A DEFINITE EVIDENCE THAT IT WAS BEHAVING IN A
18 MALIGNANT CLINICAL FASHION.
19 Q. DID ALL OF THESE PATIENTS, EXCEPT FOR THE
20 ONE FEMALE THAT YOU REFERRED TO, DIE OF METASTATIC
21 DISEASE OR DID SOME OF THEM DIE OF OTHER
22 COMPLICATIONS?
23 A. OF THE 18 PATIENTS ON THIS LIST THAT DIED,
24 ALL OF THEM DIED FROM THEIR CARCINOID TUMORS. 17
25 OF THE 18 DIED BECAUSE OF DIFFUSE SPREAD OF THE

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1 TUMOR RESULTING IN THE THINGS THAT PEOPLE WITH
2 CANCER CAN DIE FROM, LIKE CACHEXIA AND SO FORTH.
3 ONE PATIENT DIED WHO HAD A DEFINITE SPREAD OF THE
4 TUMOR TO HER MEDIASTINUM BUT DEVELOPED PRODUCTION
5 OF ACTH FROM THE TUMOR, ACTH, AND SEEMED TO HAVE A
6 -- SEEMED LIKE THAT MIGHT ALSO BE A FACTOR
7 CONTRIBUTING TO HER DEATH.
8 Q. WHICH PATIENT WAS THAT?
9 A. I'M NOT CERTAIN WHAT PATIENT THAT IS RIGHT
10 NOW. IT'S ONE OF THE FEMALE PATIENTS.
11 Q. DO YOU STILL HAVE THE RECORDS FOR EACH OF
12 THESE PATIENTS THAT ARE ON THESE COMPUTER
13 PRINT-OUT SHEETS, THE RECORDS FROM WHICH YOU
14 OBTAINED THE DATA THAT YOU FED INTO THE COMPUTER?
15 A. IS THAT A QUESTION THAT CAN BE ANSWERED?
16 Q. DO YOU UNDERSTAND IT?
17 A. I SORT OF UNDERSTAND IT.
18 Q. DO YOU STILL HAVE THE RECORDS --
19 MR. SIRRIDGE: EXCUSE ME. JUST HOW
20 ARE YOU DEFINING "RECORDS"?
21 BY MS. WALTERS:
22 Q. WELL, DOCTOR, WHERE DID YOU OBTAIN THE DATA
23 THAT WAS FED INTO THE COMPUTER FOR EACH OF THESE
24 CASES OF CARCINOID?
25 A. THIS DATA IS FROM PATIENTS I'VE SEEN OR

http://legacy.library.ucsf.edu/tid/xhn07a00/pdf
Source: https://www.industrydocuments.ucsf.edu/docs/ynxl0001

1 CONSULTED ON IN MY CAPACITY AS A PHYSICIAN.
2 Q. AND WHEN DID YOU OBTAIN THE DATA ON EACH OF
3 THESE PATIENTS?
4 A. I OBTAINED THE DATA AT VARIOUS TIMES IN THE
5 LAST 17 YEARS.
6 Q. AND WHERE DID YOU KEEP THE DATA THAT YOU
7 OBTAINED?
8 A. THE DATA IS KEPT IN MY PERSONAL COMPUTER IN
9 MY HOME.
10 Q. IN WHAT FORM?
11 A. IT'S KEPT IN THE FORM OF A DATA BASE.
12 Q. DOES YOUR DATA BASE INCLUDE A SUMMARY ON
13 EACH OF THESE PATIENTS?
14 A. IT CONTAINS SOME SELECTED INFORMATION ON
15 EACH OF THESE PATIENTS. IT IS NOT COMPLETE FOR
16 ALL FIELDS OF THE DATA BASE ON EACH PATIENT
17 BECAUSE IT WAS COLLECTED OVER 17 YEARS, AND AT
18 CERTAIN TIMES, I DIDN'T MAKE SOME OF THE
19 MEASUREMENTS. IN OTHER WORDS, I CAN OBSERVE THERE
20 ARE SOME PATIENTS THAT DON'T HAVE SEROTONIN IN
21 THEIR URINE BECAUSE AT THAT TIME I WASN'T MAKING
22 THE MEASUREMENT OR ELSE SOME I DIDN'T HAVE THE
23 PLATELET SEROTONIN BECAUSE I WASN'T MAKING THE
24 MEASUREMENT MAYBE EIGHT YEARS AGO OR WHATEVER. SO
25 THEY'RE NOT COMPLETE FOR ALL INFORMATION.

http://legacy.library.ucsf.edu/tid/xhr07a00/pdf Source: https://www.industrydocuments.ucsf.edu/docs/ynxl0001

1 Q. IF THEY'RE BLANK, DOES THAT MEAN YOU DIDN'T
2 MEASURE IT OR COULD THAT MEAN THAT IT WAS --
3 A. IF THEY'RE BLANK, THAT MEANS I DID NOT
4 MEASURE IT. ANYTHING THAT WAS AVAILABLE TO ME
5 WOULD BE ON THIS PRINT-OUT FOR THOSE SPECIFIC
6 FIELDS.
7 Q. AND DOES YOUR COMPUTER BASE ALSO CONTAIN THE
8 HISTOLOGIC DIAGNOSIS FOR EACH OF THESE TUMORS?
9 A. HISTOLOGICAL DIAGNOSIS? NO, IT DOES NOT.
10 Q. DO YOU KNOW WHAT THE HISTOLOGIC DIAGNOSIS
11 WAS FOR EACH OF THESE TUMORS THAT YOU MARKED AS
12 BENIGN BRONCHIAL CARCINOIDS?
13 A. OFFHAND, I DON'T KNOW THE HISTOLOGICAL
14 DIAGNOSIS. I KNOW THEY ALL HAD A DIAGNOSIS WHERE
15 THE PREPONDERANCE OF EVIDENCE WAS THAT THEY HAD
16 SOME TYPE OF CARCINOID TUMOR, BUT I DON'T KNOW
17 SPECIFICALLY THE HISTOLOGICAL DIAGNOSIS ON EACH
18 ONE OFFHAND.
19 Q. HOW ABOUT THE ONES THAT YOU HAVE LABELED
20 MALIGNANT BRONCHIAL TUMORS, DO YOU HAVE ANY RECORD
21 OF THE HISTOLOGIC DIAGNOSIS FOR EACH OF THOSE?
22 A. THAT INFORMATION IS NOT IN MY DATA BASE, THE
23 HISTOLOGICAL. THERE'S NO ENTRY FOR THE
24 HISTOLOGICAL DIAGNOSIS, FOR SPECIFICALLY A
25 HISTOLOGICAL DIAGNOSIS.

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Source: https://www.industrydocuments.ucsf.edu/docs/ynxl0001

1 Q. WERE ALL OF THESE PATIENTS HISTOLOGICALLY
2 DIAGNOSED?
3 A. THEY WERE ALL, TO MY RECOLLECTION,
4 HISTOLOGICALLY DIAGNOSED. IT'S BEEN -- OVER THE
5 YEARS ONLY THE MOST -- I CAN'T RECALL ANY OF THESE
6 THAT WEREN'T.
7 Q. WERE THEY ALL HISTOLOGICALLY DIAGNOSED AT
8 DUKE UNIVERSITY MEDICAL CENTER?
9 A. NOT ALL HISTOLOGICALLY DIAGNOSED AT DUKE
10 MEDICAL CENTER, FOR INSTANCE. FOR INSTANCE, THERE
11 WAS ONE THAT WAS DIAGNOSED AT ANOTHER MEDICAL
12 CENTER BY A VERY COMPETENT PATHOLOGIST WHO SENT ME
13 HIS REPORT.
14 Q. DO YOU KNOW WHAT MEDICAL CENTER THAT WAS?
15 A. I FEEL LIKE THAT'S A PRIVILEGED
16 COMMUNICATION BETWEEN ME AND MY PATIENTS AND I
17 DON'T KNOW THAT THAT'S RELEVANT TO THIS BECAUSE
18 THESE PATIENTS AREN'T ACTUALLY A PART OF THIS
19 CASE.
20 Q. IS IT ANOTHER DOCTOR THAT'S INVOLVED IN THIS
21 CASE?
22 A. OH, NO, OH, NO.
23 Q. IS IT ANOTHER MEDICAL CENTER THAT'S INVOLVED
24 IN THIS CASE?
25 A. NO.

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1 Q. BY VIRTUE OF HAVING ONE OF ITS EXPERTS
2 TESTIFY IN THIS CASE?
3 A. NO, ABSOLUTELY NOT.
4 Q. OTHER THAN THAT ONE, ARE THERE ANY OTHERS
5 THAT WERE HISTOLOGICALLY DIAGNOSED OUTSIDE OF DUKE
6 UNIVERSITY MEDICAL CENTER?
7 A. THIS IS AGAIN FROM MY RECOLLECTION, SOME OF
8 THEM INITIALLY WOULD HAVE BEEN HISTOLOGICALLY
9 DIAGNOSED AT THE MEDICAL CENTER, ANOTHER MEDICAL
10 CENTER, BUT IT'S MY GENERAL PRACTICE, ALTHOUGH I
11 CAN'T SAY IT WAS DONE ABSOLUTELY IN EVERY CASE, TO
12 TRY TO OBTAIN THE SLIDES, AND IT'S ALSO THE
13 PRACTICE OF THE OTHER DOCTORS AT DUKE TO TRY TO
14 OBTAIN THE SLIDES AND HAVE THEM REVIEWED BY THE
15 PATHOLOGIST AT DUKE TO SEE IF THEY CONFIRM THE
16 DIAGNOSIS. AND THAT'S BEEN DONE IN THE MAJORITY
17 OF THE CASES, ALTHOUGH I CAN'T FROM MY MEMORY SAY
18 IT'S BEEN DONE IN ABSOLUTELY EVERY ONE THAT SLIDES
19 WERE REVIEWED BY DUKE. BUT IN EACH CASE, IT HAD
20 TO BE REVIEWED BY SOMEONE THAT WOULD, I THINK TO
21 BE, A QUALIFIED PERSON TO REVIEW THEM.
22 Q. WERE THE MAJORITY OF THESE CARCINOIDS
23 HISTOLOGICALLY DIAGNOSED AT DUKE MEDICAL CENTER?
24 A. WHAT DO YOU MEAN BY "DIAGNOSED"? DO YOU
25 MEAN AS FAR AS THE TISSUE OR --

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1 Q. THE TUMOR HISTOLOGICALLY DIAGNOSED AS BEING
2 A CARCINOID AT DUKE MEDICAL CENTER?
3 A. THE MAJORITY OF THE TUMORS WOULD HAVE BEEN
4 HISTOLOGICALLY DIAGNOSED AT THE MEDICAL CENTER,
5 YES, ALTHOUGH INITIALLY THEY MAY HAVE BEEN
6 DIAGNOSED AT ANOTHER MEDICAL CENTER AND THE
7 PATIENT CAME AND THEY BROUGHT THE SLIDES.
8 Q. WOULD THE MAJORITY HAVE BEEN ORIGINALLY
9 DIAGNOSED AT DUKE MEDICAL CENTER?
10 A. I DON'T HAVE ANY WAY OF KNOWING THAT.
11 THAT'S NOT PART OF MY DATA BASE. THE THING IS IF
12 -- THE MAIN TEST IS IF THEY COME TO DUKE CENTER AT
13 SOME TIME FOR THEIR MEDICAL CARE, THEN I CONSIDER
14 THEM AT DUKE, BUT I DON'T HAVE THE DATA
15 SPECIFICALLY IF THEY WERE.
16 Q. IN ANY EVENT IF THEY WERE PRINCIPALLY
17 DIAGNOSED OR PRIMARILY DIAGNOSED SOMEWHERE ELSE,
18 THE DIAGNOSIS WOULD HAVE BEEN CONFIRMED BY DUKE
19 MEDICAL CENTER, IS THAT CORRECT?
20 A. IN THE MAJORITY OF THE PATIENTS, IT WOULD
21 HAVE BEEN CONFIRMED BY A PATHOLOGIST AT DUKE
22 MEDICAL CENTER, IF WE COULD OBTAIN THE SLIDES OR
23 IF THE PATIENT HAPPENED TO HAVE A SECOND BIOPSY OR
24 SOMETHING, BUT I CAN'T SAY ABSOLUTELY THAT THEY
25 ALL WERE.

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1 Q. BUT YOU DON'T KNOW WHAT THE HISTOLOGIC
2 DIAGNOSIS WAS FOR THESE?
3 A. I DON'T KNOW SPECIFICALLY WHAT IT WAS. THEY
4 ALL WERE -- THEY WERE ALL THE PREPONDERANCE OF
5 PATHOLOGICAL DIAGNOSIS WAS THAT THEY HAD SOME FORM
6 OF A CARCINOID TUMOR. HOW DO YOU MEAN WHAT THE
7 HISTOLOGICAL DIAGNOSIS WAS?
8 MS. WALTERS: DO YOU WANT TO FINISH
9 UP THIS AREA OR --
10 MR. NORTHRIP: WE WANT TO DO WHAT YOU
11 WANT TO DO.
12 MS. WALTERS: LET'S FINISH UP THIS
13 AREA.
14 THE WITNESS: OKAY.
15 BY MS. WALTERS:
16 Q. DOES DUKE UNIVERSITY MEDICAL CENTER USE --
17 WELL, DO YOU KNOW -- STRIKE THAT.
18 LET ME START AGAIN. DO YOU KNOW WHAT
19 CLASSIFICATION SYSTEM DUKE UNIVERSITY PATHOLOGY
20 DEPARTMENT USES TO HISTOLOGICALLY DIAGNOSE
21 CARCINOIDS?
22 MR. SIRRIDGE: THE FORM OF THE
23 QUESTION, CARCINOIDS OF --
24 BY MS. WALTERS:
25 Q. OF THE LUNG. WHY DON'T WE DO THAT.

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1 A. WELL, THERE'S A VARIETY OF PATHOLOGISTS AT
2 DUKE UNIVERSITY MEDICAL CENTER WHO ROTATE ON
3 INTERPRETING SURGICAL SECTIONS AND EVEN AUTOPSY
4 SECTIONS. AND THEY WILL BE ON SERVICE FOR A WEEK
5 AND THEN THEY'LL GO OFF THE SERVICE AND, OF
6 COURSE, OVER THE 17 YEARS THAT I'VE HAD AN
7 OPPORTUNITY TO COLLECT THIS DATA WOULD HAVE BEEN A
8 VARIETY OF PATHOLOGISTS. SOME ARE STILL AT DUKE
9 AND SOME ARE GONE. AND THEY USE A VARIETY OF
10 TERMS IN TRYING TO CLASSIFY CARCINOID TUMORS.
11 Q. WHAT TERMS DO THEY USE?
12 A. WELL, THE MOST COMMON TERM THEY USE IS A
13 BRONCHIAL CARCINOID TUMOR. THAT'S NUMBER ONE.
14 SOME OF THEM USE THE TERM TYPICAL BRONCHIAL
15 CARCINOID TUMOR SOMETIMES SYNONYMOUSLY WITH
16 BRONCHIAL CARCINOID TUMOR AS FAR AS MY
17 UNDERSTANDING. SOME OF THEM USE THE TERM ATYPICAL
18 BRONCHIAL CARCINOID TUMOR. SOME OF THEM USE THE
19 TERM MALIGNANT BRONCHIAL CARCINOID TUMOR. AND,
20 FINALLY, SOME OF THEM USE A TERM, AND I CAN'T TELL
21 YOU THE PRECISE VARIATIONS, BUT THEY'RE ALONG THE
22 LINE OF NEUROENDOCRINE TUMOR OF THE LUNG. SOME OF
23 THEM USE THAT.
24 Q. DO THEY USE THAT WITHOUT ANY QUALIFICATIONS?
25 A. PARDON?

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1 Q. DO THEY USE THAT TERMINOLOGY WITHOUT ANY
2 QUALIFICATIONS?
3 A. SOMETIMES THEY WILL CALL IT A -- SEEMS THIS
4 IS FROM MY RECOLLECTION -- POORLY DIFFERENTIATED
5 NEUROENDOCRINE TUMOR OR A MALIGNANT NEUROENDOCRINE
6 TUMOR. I'M NOT SURE HOW THEY QUALIFY THEM FROM
7 TIME TO TIME. THAT SORT OF DEFIES MY
8 RECOLLECTION.
9 Q. DO YOU KNOW WHAT EACH OF THOSE TERMS MEANS
10 FROM A PATHOLOGICAL VIEWPOINT?
11 A. WELL, FROM WORKING WITH THEM, OF COURSE, I'M
12 NOT A PATHOLOGIST AND I'M NOT AN EXPERT IN
13 PATHOLOGY, BUT FROM WORKING WITH THEM AS A
14 CLINICIAN, I'VE HAD TO TRY TO AND SOMETIMES ON
15 EACH OCCASION TO ASK THEM WHAT THEY MEAN WHEN THEY
16 USE THOSE TERMS AND TO MAKE CERTAIN THAT WE'RE
17 TALKING ABOUT SOMETHING THAT WE ALL UNDERSTAND.
18 SO I CAN'T SAY THAT EACH PATHOLOGIST USES THE TERM
19 IN EXACTLY THE SAME MANNER BECAUSE OF THE WAY THE
20 PATHOLOGY DEPARTMENT IS SET UP.
21 Q. SOME OF THESE TERMS MAY HAVE DIFFERENT
22 MEANINGS TO DIFFERENT PATHOLOGISTS?
23 A. I WOULD MORE PHRASE IT TO SAY THAT SOMETIMES
24 THE DIFFERENT PATHOLOGISTS USE DIFFERENT TERMS FOR
25 THE SAME THING. YOU HAVE TO JUST MAKE SURE WHAT

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1 THEY'RE TALKING ABOUT BY TALKING TO THEM.
2 SOMETIMES THEY WILL WRITE A COMMENT ON THE
3 PATHOLOGY REPORT, AFTER THE DESCRIPTION OF THE
4 TISSUE AND THE DIAGNOSIS, THEY'LL WRITE A COMMENT
5 TO EXPLAIN WHAT THEIR TERM MEANT IN RELATIONSHIP
6 TO THAT PARTICULAR SPECIMEN THEY EVALUATED.
7 Q. BUT YOU HAVE NO WAY OF KNOWING WHICH ONE OF
8 THESE TERMS OR WHICH ONE OF THESE HISTOLOGIC
9 DIAGNOSES WERE GIVEN TO WHICH OF THESE CARCINOIDS
10 THAT YOU HAVE LISTED ON YOUR COMPUTER PRINT-OUT;
11 IS THAT CORRECT?
12 A. NO, I DON'T KNOW SPECIFICALLY WHICH ONE WAS
13 LISTED WITH EACH TISSUE, THAT IS CORRECT. I
14 DIDN'T DO THAT WITH THAT GOAL IN MIND ACTUALLY. I
15 DIDN'T MAKE THE PRINT-OUT WITH THAT GOAL IN MIND
16 SO MUCH.
17 Q. WHAT WAS YOUR GOAL IN MAKING THIS PRINT-OUT?
18 A. MY GOAL IN MAKING THIS PRINT-OUT IS THAT
19 WHILE READING A COPY OF THE EXPERT TESTIMONY OF
20 ONE OF THE WITNESSES, I SAW A STATEMENT THAT THE
21 WITNESS MADE THAT DIDN'T REALLY AGREE WITH MY
22 RECOLLECTIONS OF MY PERSONAL EXPERIENCE AND I MADE
23 THIS PRINT-OUT REALLY OUT OF CURIOSITY TO TRY AND
24 SEE, SCIENTIFIC CURIOSITY ABOUT WHETHER, IN FACT,
25 MY RECOLLECTIONS WERE RELATIVELY CORRECT.

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1 Q. WHICH WITNESS WAS THAT?

2 A. THAT WOULD BE THE EXPERT TESTIMONY OF DR.

3 MILLS FROM, I BELIEVE, THE MEDICAL COLLEGE OF

4 VIRGINIA.

5 Q. AND WHAT WAS THE STATEMENT THAT YOU READ?

6 A. I READ IN HIS EXPERT TESTIMONY WHILE

7 DISCUSSING ATYPICAL CARCINOID TUMORS THAT HE FELT

8 IT WAS EXTREMELY UNCOMMON IN HIS EXPERIENCE TO

9 HAVE A PATIENT WHO HAD AN ATYPICAL CARCINOID TUMOR

10 WHO DID NOT HAVE A HISTORY OF SIGNIFICANT

11 CIGARETTE SMOKING. AND I COULD LOOK AT THIS

12 EXPERT WITNESS, BUT IT SEEMS LIKE THE RECOLLECTION

13 IS HE SAID HE COULDN'T EVER RECALL HAVING SEEN --

14 HAVING EVER PERSONALLY EVALUATED TISSUE FROM SUCH

15 A PATIENT. AND THAT DID NOT -- THAT WAS DIFFERENT

16 THAN MY RECOLLECTION OF MY EXPERIENCE OVER THE 17

17 YEARS.

18 Q. AND DOES THIS IN ANY WAY CLARIFY WHAT YOUR

19 EXPERIENCE IS OVER THE YEARS?

20 A. I THOUGHT IT DID.

21 Q. MEANING P-3?

22 A. P-3, DOES P-3 REFER TO ALL THE PAGES IN IT?

23 Q. YES.

24 A. WELL, IT SORT OF WAS JUST SOMETHING I DID ON

25 MY OWN JUST TO TRY AND SATISFY MY CURIOSITY AND I

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1 FELT LIKE IT DID CLARIFY SOMEWHAT FOR ME WHAT I
2 HAD REMEMBERED IN THAT I DID FIND A SUBSTANTIAL
3 NUMBER OF PATIENTS THAT HAD -- THAT DID NOT HAVE A
4 HISTORY OF SMOKING AT ALL OR A HISTORY OF
5 SIGNIFICANT EXPOSURE TO CIGARETTES. SO I THINK IT
6 DID, IN MY OWN MIND FOR MY OWN CURIOSITY, IT DID
7 SORT OF SATISFY ME IN THAT RESPECT.
8 Q. BUT YOU HAVE NO WAY OF CORRELATING, AS I
9 UNDERSTAND IT, YOUR SMOKING HISTORIES WITH
10 PATIENTS THAT HAD HISTOLOGIC DIAGNOSES OF ATYPICAL
11 CARCINOID? AND ATYPICAL CARCINOID THERE IS USED
12 AS A PATHOLOGIST WOULD USE IT.
13 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
14 WHICH PATHOLOGIST?
15 MS. WALTERS: WELL, IN THE PATHOLOGY
16 LITERATURE, I GUESS, WE'D HAVE TO SAY.
17 THE WITNESS: WELL, THE WAY THE
18 PATHOLOGISTS USE THE TERM, TO MY UNDERSTANDING AS
19 A COMMON EXPERT IS IN PATHOLOGY, IS THEY USE THE
20 TERM IN DESCRIBING WHAT THEY SEE UNDER THE
21 MICROSCOPE AND WHAT THEY MIGHT SEE GROSSLY. WHAT
22 I'M INTERESTED IN AS A CLINICIAN IS DOES THAT TERM
23 HELP ONE PREDICT HOW A GIVEN PATIENT IS GOING TO
24 FARE IN THE FUTURE AS FAR AS THIS TUMOR POSSIBLY
25 RECURRING BECAUSE I THINK THAT ALL THE TUMORS HAVE

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1 AT LEAST SOME POTENTIAL TO RECUR, AT LEAST THAT'S
2 THE WAY I HAVE TO CONSIDER THEM.
3 OVER THE YEARS, I'VE SEEN PATIENTS
4 THAT HAVE HAD A DIAGNOSIS OF ATYPICAL CARCINOID
5 THAT NEVER CAME BACK. AND, ON THE OTHER HAND,
6 I'VE SEEN PATIENTS THAT HAVE A DIAGNOSIS OF
7 TYPICAL BRONCHIAL CARCINOID THAT DID COME BACK.
8 SO I TOOK THIS AS SORT OF -- I USED MY TERM BENIGN
9 AND MALIGNANT MORE OR LESS TO DESCRIBE THE
10 CLINICAL COURSE IN MY OWN MIND TO SEE IF AS A
11 CLINICIAN, THE TYPICAL AND ATYPICAL TERMS, YOU
12 KNOW, BORE ANY RELATIONSHIP TO MY CLINICAL
13 EXPERIENCE.
14 BY MS. WALTERS:
15 Q. BUT YOU HAD NO WAY TO CORRELATE THE SMOKING
16 HISTORY WITH THE HISTOLOGIC DIAGNOSIS IN ANY OF
17 THOSE PATIENTS?
18 A. I DID NOT.
19 MS. WALTERS: WHY DON'T WE TAKE OUR
20 LUNCHEON BREAK NOW AND WE'LL COME BACK IN AN
21 HOUR.
22 (LUNCHEON RECESS)
23 BY MS. WALTERS:
24 Q. DOCTOR, LOOKING BACK AT P-3, WHICH IS THE
25 COMPUTER PRINT-OUT, YOU HAVE SMOKING HISTORY IN

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1 PACK YEARS GIVEN FOR SOME OR ALL OF THESE
2 CARCINOIDS. WHAT DO THE ZEROS REPRESENT?
3 A. THE ZEROS UNDER PACK YEARS REPRESENTS THEY
4 HAD NO HISTORY OF SMOKING, THAT THEY NEVER HAD
5 SMOKED.
6 Q. DID THEY HAVE A HISTORY OF NOT SMOKING?
7 A. YES, THEY RESPONDED TO A QUESTION DO YOU
8 SMOKE SAYING NO, NEVER SMOKED OR I DON'T SMOKE, I
9 NEVER SMOKED.
10 Q. WHAT WAS THE QUESTION, DO YOU SMOKE OR HAVE
11 YOU EVER SMOKED?
12 A. THE QUESTION WAS: HAVE YOU EVER SMOKED?
13 Q. HOW DO YOU KNOW THAT WAS THE QUESTION THEY
14 RESPONDED TO?
15 A. THAT IS GENERALLY THE WAY THAT THE DOCTORS
16 AT DUKE ARE INSTRUCTED TO ASK THEM QUESTIONS ABOUT
17 SMOKING.
18 Q. WHERE DID YOU GET THIS INFORMATION FROM?
19 A. I GOT THIS INFORMATION IN MANY CASES FROM
20 MYSELF ASKING THE PATIENT DID YOU EVER SMOKE. IN
21 CASES WHERE I DIDN'T GET IT MYSELF ASKING THE
22 PATIENT, I GOT IT FROM THE MEDICAL RECORD WHERE
23 THERE'S A PLACE WHERE THEY'RE ASKED BY THE INTERN
24 OR THE RESIDENT, DID YOU EVER SMOKE OR DO YOU
25 SMOKE --

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1 Q. IS THAT QUESTION WRITTEN ON THE RECORD?
2 A. IT IS WRITTEN ON THE RECORD. I CAN'T
3 REMEMBER THE EXACT WORDS IT IS WRITTEN IN, BUT
4 IT'S UNDER DO YOU DRINK, DO YOU SMOKE TYPE OF
5 THING. AND DUKE DOCTORS ARE INSTRUCTED THAT IF
6 SOMEONE DOESN'T SMOKE, THEY'RE SUPPOSED TO ASK
7 THEM -- THEY'RE SUPPOSED TO ASK THEM IF THEY EVER
8 SMOKED AND IF THEY ASK THEM IF THEY DID SMOKE AT
9 ONE TIME, THEY'RE SUPPOSED TO ASK THEM WHEN THEY
10 STOPPED SMOKING.
11 Q. HOW LONG HAS THIS BEEN THE PRACTICE AT DUKE
12 MEDICAL CENTER?
13 A. IT'S BEEN THE PRACTICE AS LONG AS I'VE BEEN
14 THERE AND I'VE BEEN THERE 20 YEARS NOW. IT'S BEEN
15 THE PRACTICE THAT LONG AND IT'S BEEN THE PRACTICE
16 IN THE LAST 17 YEARS. IT'S BEEN THE PRACTICE AS
17 LONG AS THIS DATA HAS BEEN COLLECTED.
18 Q. JUST BY LOOKING AT THE RECORD FROM WHICH YOU
19 TOOK THE SMOKING HISTORIES, WOULD YOU HAVE ANY WAY
20 OF KNOWING WHETHER THE DOCTOR, IN FACT, ASKED THE
21 PATIENT HAVE YOU EVER SMOKED?
22 (OBJECTION) MR. SIRRIDGE: I'M GOING TO OBJECT TO
23 THE FORM. HE SAID HE PERSONALLY ASKED.
24 MS. WALTERS: SOME OF THEM.
25 THE WITNESS: SOME OF THEM.

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1 MS. WALTERS: OTHERS HE TOOK FROM THE
2 RECORD.
3 BY MS. WALTERS:
4 Q. JUST BASED ON LOOKING AT THE RECORD OF THOSE
5 PATIENTS, WOULD YOU HAVE ANY WAY OF KNOWING
6 WHETHER THE DOCTOR, IN FACT, ASKED THE PATIENTS
7 WHETHER THEY EVER SMOKED?
8 A. WELL, WHAT I DID WAS WHEN I DIDN'T
9 PERSONALLY ASK THEM THE QUESTION AND RECORD IT IN
10 MY OWN NOTES, I LOOKED WHENEVER I COULD, AND THIS
11 WAS IN LARGE PERCENTAGES, I LOOKED IN AT LEAST TWO
12 DIFFERENT TIMES THEY WERE ADMITTED TO SEE IF THERE
13 WAS A CONCURRENCE THAT BOTH TIMES THEY DIDN'T
14 SMOKE OR THEY SMOKED FIVE YEARS OR TEN YEARS BY
15 TWO INDEPENDENT DIFFERENT DOCTORS. AND THE
16 DOCTORS AT DUKE ARE REALLY VERY COMPULSIVE AND
17 METICULOUS, THE RESIDENTS AND INTERNS, AND WE HAVE
18 QUITE A SELECTION FACTOR, AND ESPECIALLY IF TWO
19 DOCTORS RECORDED THE SAME THING, I THINK IT'S
20 EXTREMELY LIKELY THAT THE INFORMATION IS -- THAT
21 THEY DID ASK THEM THE QUESTION.
22 Q. THE TWO DOCTORS RECORDED SMOKING INFORMATION
23 ON EACH AND EVERY ONE OF THESE PATIENTS?
24 A. NOT ON EVERY ONE. AS MANY AS I COULD SEE
25 THAT WERE IN MORE THAN ONE TIME AND THAT WAS A

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1 GOOD PERCENTAGE. I'D SAY AT LEAST HALF AS MANY AS
2 THAT WERE IN MORE THAN ONE TIME. IF I DIDN'T ASK
3 MYSELF, I WOULD LOOK AT THE DIFFERENT ADMISSIONS
4 TO MAKE SURE THAT THE INFORMATION ABOUT SMOKING
5 WAS CONSISTENT. SOMETIMES WHEN SOMEONE WAS JUST
6 IN ONE TIME, THEN IT WASN'T -- IT WAS ONLY ONE
7 TIME. NOW, MANY TIMES THE INTERN AND THE RESIDENT
8 ON WOULD ASK THE QUESTION IN DIFFERENT PARTS OF
9 THE HISTORY AND PHYSICAL FORM, AND I WOULD LOOK AT
10 BOTH THE INTERN AND THE RESIDENT'S RESPONSE THAT
11 THEY RECORDED THAT THE PATIENT STATED. SO WITHIN
12 THE LIMITS THAT I COULD, I TRIED TO CHECK -- I TRY
13 TO CHECK IT CAREFULLY THAT IT WAS ACCURATE. AND
14 IN A SUBSTANTIAL NUMBER, I RECORDED IT MYSELF AND
15 ASKED.
16 Q. DO YOU HAVE ANY WAY OF RECREATING WHICH OF
17 THESE PATIENTS YOU PERSONALLY ASKED, WHICH YOU
18 OBTAINED THE INFORMATION BY ONE ENTRY ON THE CHART
19 AND WHICH YOU OBTAINED BY TWO ENTRIES ON THE
20 CHART?
21 A. IT COULDN'T BE DONE REAL EASILY, BUT
22 PROBABLY AT LEAST FOR SOME IT COULD BE DONE. IT
23 ISN'T SOMETHING I COULD GO TO MY COMPUTER AND DO
24 IT BECAUSE I FINALLY TOOK WHAT APPEARED TO BE THE
25 BEST INFORMATION I HAD AND THAT WAS ENTERED INTO

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1 THE COMPUTER AS IT WAS.

2 Q. DOCTOR, WHAT ARE THE DIFFERENT WAYS THAT A

3 TUMOR PRODUCES SEROTONIN? WHAT ARE THE DIFFERENT

4 FORMS THAT A TUMOR PRODUCES SEROTONIN?

5 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.

6 BY MS. WALTERS:

7 Q. IS THAT FORM IMPROPER?

8 A. WELL --

9 Q. IS THAT MEDICALLY CORRECT?

10 A. IT'S NOT MEDICALLY CORRECT TO STATE IT IN

11 THAT SOMETIMES THE TUMOR CANNOT PRODUCE

12 SEROTONIN. IT PRODUCES A PRECURSOR OF SEROTONIN

13 SO --

14 Q. WHAT PRODUCES SEROTONIN?

15 A. WHAT PRODUCES SEROTONIN? OKAY. SEROTONIN

16 IS PRODUCED WHEN THE AMINO ACID, TRYPTOPHAN, IS

17 CONVERTED TO 5-HYDROXYTRYPTOPHAN --

18 Q. IS THAT ALSO 5-HT?

19 A. 5-HTP, IF YOU WANT TO CALL IT THAT, I CAN

20 USE THAT TERM FOR NOW ON TO SAVE TIME, IS

21 CONVERTED TO 5-HTP BY AN ENZYME, TRYPTOPHAN

22 HYDROXYLASE. AND THE TRYPTOPHAN HYDROXYLASE IS

23 FOUND IN SOME CARCINOID TUMORS IN THE BRAIN. NOW,

24 THE 5-HYDROXYTRYPTOPHAN IS THEN CHANGED TO

25 SEROTONIN BY THE ENZYME AROMATIC AMINO-ACID

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1 DECARBOXYLASE.

2 Q. COULD YOU REPEAT THAT WORD, AGAIN?

3 A. AROMATIC AMINO-ACID DECARBOXYLASE. WE

4 COMMONLY ABBREVIATE IT AS DOPA. OUR ABBREVIATION

5 OF ANY VALUE HERE TO SAVE SOME TIME --

6 Q. YES. WHAT'S THE ABBREVIATION FOR THAT, JUST

7 DOPA?

8 A. DOPA DECARBOXYLASE. IT'S CALLED THAT

9 BECAUSE OF THE SAME ENZYME, DECARBOXYLASE, DOPA.

10 AND THEN THE SEROTONIN IS FORMED AND THEN IT

11 GENERALLY CAN BE TAKEN UP AND STORED IN SOME

12 TISSUES OF THE BODY SUCH AS THE PLATELETS.

13 Q. IS THAT IN THE BLOOD?

14 A. THE PLATELETS ARE IN THE BLOOD. AND THEN IT

15 GOES TO THE TISSUES OF THE BODY WHERE IT MIGHT

16 EXERT ITS PHYSIOLOGICAL EFFECT OR PHARMACOLOGICAL

17 EFFECT AND THEN IT'S THEN INACTIVATED FROM

18 SEROTONIN THROUGH AN INTERMEDIATE, WHICH ISN'T OF

19 CRITICAL IMPORTANCE, ULTIMATELY THROUGH THE 5-HIAA

20 WE TALKED ABOUT. AND IT'S INACTIVATED BY AN

21 ENZYME CALLED MONOAMINE OXIDASE, M-O-N-O-A-M-I-N-E

22 O-X-I-D-A-S-E, ABBREVIATED VERY COMMONLY AS

23 CAPITAL MAO. AND THIS 5-HIAA IS THEN EXCRETED IN

24 THE URINE OF THE PATIENT.

25 Q. AND, DOCTOR, IS THE ENZYME TRYPTOPHAN

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1 HYDROXYLASE FOUND IN CARCINOIDS OF THE LUNG?
2 A. IT IS FOUND IN SOME CARCINOID TUMORS OF THE
3 LUNG BUT NOT ALL CARCINOID TUMORS OF THE LUNG.
4 Q. IS IT FOUND IN SOME SMALL CELL CANCERS OF
5 THE LUNG?
6 A. I CANNOT TO MY RECOLLECTION REMEMBER ANYONE
7 WHO HAS DEMONSTRATED IT IN SMALL CELL CARCINOMAS
8 OF THE LUNG OR ATTEMPTED TO DO IT OR DEMONSTRATE
9 IT IN THERE. THAT TYPE OF EXPERIMENT ISN'T DONE
10 REAL OFTEN.
11 Q. SO IT HASN'T BEEN EXPLORED WITH RESPECT TO
12 SMALL CELL CANCER?
13 A. I DON'T KNOW IF IT'S BEEN EXPLORED AND NOT
14 FOUND OR HASN'T BEEN EXPLORED. I HONESTLY DON'T
15 KNOW THAT OFF THE TOP OF MY HEAD FROM THE
16 INFORMATION THAT I CARRY WITH ME. I CAN'T RECALL
17 IT. I KNOW IT'S DEMONSTRATED IN SOME, SOME
18 CARCINOID TUMORS, BUT NOT ALL.
19 Q. IS FIVE -- IS THERE A TEST FOR 5-HTP?
20 A. THERE ARE SOME TESTS FOR 5-HTP.
21 Q. ARE THOSE TESTS THAT YOU DO?
22 A. I HAVE AND AM CAPABLE OF DOING TESTS FOR
23 5-HTP ALTHOUGH I DON'T ALWAYS DO THEM.
24 Q. HAVE YOU EVER DONE THEM IN ANY OF THE THREE
25 RESEARCH ARTICLES THAT WE'VE DISCUSSED HERE TODAY?

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1 A. YES, I HAVE. I DID THEM AS PART OF THE
2 ARTICLE IN CLINICAL CHEMISTRY.
3 Q. AND YOU DID THAT ON THE CARCINOIDS IN THAT
4 STUDY; IS THAT CORRECT?
5 A. I DID THAT ON THE CARCINOIDS IN THAT STUDY,
6 THAT IS CORRECT.
7 Q. BUT NOT ON ANY OF THE SMALL CELL CANCERS?
8 A. TO MY RECOLLECTION, I DID NOT DO THEM ON ANY
9 OF THE SMALL CELL CANCERS. AT LEAST I DIDN'T DO
10 THEM AND PUT THEM IN THE PAPER. I CAN'T
11 ABSOLUTELY SAY I DIDN'T DO THEM BECAUSE THE THRUST
12 OF THE PAPER WAS TO THE CARCINOID TUMORS AND SO I
13 WAS TRYING TO MAKE A POINT ABOUT THE 5-HTP AND ITS
14 RELATIONSHIP TO SEROTONIN IN CARCINOID TUMOR
15 PATIENTS SO --
16 Q. IS TRYPTOPHAN FOUND IN CARCINOID TUMORS, THE
17 AMINO ACID TRYPTOPHAN?
18 A. THE AMINO ACID TRYPTOPHAN IS AN AMINO ACID
19 THAT IS ACTUALLY FOUND IN A LOT OF TISSUES AND,
20 INDEED, IN THE BLOOD STREAM IN THE PLASMA AND SO
21 FORTH. IT'S A FAIRLY COMMON AMINO ACID.
22 Q. IS THAT FOUND IN NORMAL TISSUES?
23 A. YES, IT IS. IT'S FOUND IN NORMAL TISSUES, A
24 CONSTITUENT OF NORMAL TISSUES.
25 Q. IS IT FOUND IN NORMAL LUNG TISSUE?

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1 A. I'M QUITE SURE IT WOULD BE FOUND IN NORMAL
2 LUNG TISSUE. I CAN'T CITE A REFERENCE BUT IT'S
3 BEEN FOUND IN VIRTUALLY EVERY TISSUE IF THE PERSON
4 IS NOT DEFICIENT IN THE TRYPTOPHAN. I BELIEVE
5 IT'S AN ESSENTIAL AMINO ACID AND SO YOU HAVE TO
6 TAKE IT IN YOUR DIET, AT LEAST IN HUMANS.
7 Q. IS 5-HTP ONLY FOUND WHEN TRYPTOPHAN IS
8 CONVERTED TO THAT SUBSTANCE OR IS THERE ANOTHER
9 WAY THAT 5-HTP CAN BE FORMED?
10 A. TO MY KNOWLEDGE, THE ONLY WAY THAT 5-HTP IS
11 FORMED IS IF TRYPTOPHAN IS CONVERTED INTO THE
12 5-HTP.
13 Q. SO YOU NEED THE ENZYME TRYPTOPHAN
14 HYDROXYLASE IN ORDER TO GET HTP; IS THAT CORRECT?
15 A. WELL, THAT'S PARTIALLY CORRECT. OF COURSE,
16 YOU COULD GET IT IF IT WAS PRODUCED IN ONE TISSUE
17 BY -- IF IT WAS PRODUCED IN ONE TISSUE BY THAT
18 ENZYME, TRYPTOPHAN HYDROXYLASE, AND THEN
19 TRANSPORTED, LET'S SAY, THROUGH THE BLOOD TO
20 ANOTHER TISSUE, PERHAPS COULD GET INTO THAT TISSUE
21 EVEN THOUGH IT ISN'T PRODUCED THERE. IT'S SORT OF
22 EXPORTED.
23 Q. SO, IN OTHER WORDS, YOU NEED TO HAVE THE
24 ENZYME TRYPTOPHAN HYDROXYLASE IN SOME PART OF THE
25 BODY IN ORDER TO GET 5-HTP?

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1 A. I WOULD SAY THAT IS CORRECT. TO MY
2 KNOWLEDGE, IT'S NOT A NORMAL CONSTITUENT OF FOODS
3 THAT I'M AWARE OF SO THAT ONE COULD EAT IT LIKE
4 YOU CAN TRYPTOPHAN AND GET IT. IT SEEMS LIKE IT
5 HAS TO BE PRODUCED IN THE BODY. FOODS THAT I'VE
6 -- I'VE LOOKED FOR IT IN FOODS,
7 5-HYDROXYTRYPTOPHAN. I'VE LOOKED IN CERTAIN FOODS
8 AND I HAVEN'T FOUND IT.
9 Q. WHEN YOU FIND 5-HTP BY TESTING AN INDIVIDUAL
10 WITH A LUNG TUMOR, WHAT DOES THAT MEAN?
11 A. THE PATIENT WITH A LUNG TUMOR --
12 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
13 THE WITNESS: YOU MEAN WHERE YOU FIND
14 IT IN A -- I SHOULD CLARIFY IT TO SAY THAT IF ONE
15 USES EXTREMELY SENSITIVE METHODS, WHICH I HAVE NOT
16 USED, ONE MAY BE ABLE TO DEMONSTRATE AT EXTREMELY
17 LOW LEVELS IN NORMAL PEOPLE, BUT IT'S EXTREMELY,
18 EXTREMELY LOW, AND I'VE NEVER ATTEMPTED TO MEASURE
19 IT. IN OTHER WORDS, THERE IS A TINY AMOUNT OF IT,
20 5-HYDROXYTRYPTOPHAN EVEN IN THE URINE OF NORMAL
21 PEOPLE SO IT'S BEING PRODUCED IN ALL OF US AND
22 THAT'S HOW WE PROBABLY GET OUR SEROTONIN. BUT SO
23 I THINK ONE WOULD HAVE TO SAY YOU'RE LOOKING AT
24 ABNORMALLY HIGH AMOUNTS IN ILLNESSES AND DISEASE
25 STATES.

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1 BY MS. WALTERS:

2 Q. SO THAT MEANS THAT ALL HUMAN BEINGS HAVE

3 SOME OF THE ENZYME TRYPTOPHAN HYDROXYLASE IN THEIR

4 BODY; IS THAT CORRECT?

5 A. THEY HAVE IT SOMEWHERE IN THEIR BODY

6 PROBABLY, YES, YES, IN THEIR INTESTINAL TRACT OR

7 SOMEWHERE IN THEIR BODY.

8 Q. AND WHEN YOU FIND AN ELEVATED LEVEL OF 5-HTP

9 IN A PATIENT WITH A LUNG TUMOR, WHAT SIGNIFICANCE

10 IS THAT?

11 A. WELL, THE SIGNIFICANCE WOULD BE THAT ONE

12 WOULD -- THE ASSUMPTION WOULD BE IF THERE'S A HIGH

13 LEVEL IN A PATIENT WITH A LUNG TUMOR, OR ANY KIND

14 OF TUMOR, THAT THE TUMOR IS PROBABLY MANUFACTURING

15 IT WOULD BE THE ASSUMPTION THAT I WOULD MAKE.

16 Q. AND IS THERE ANY PURPOSE FOR -- USEFUL

17 PURPOSE FOR FINDING OUT THAT INFORMATION?

18 A. YES. ELEVATED LEVELS OF 5-HYDROXYTRYPTOPHAN

19 ARE MEASURED BECAUSE THEY ARE ELEVATED IN THE

20 URINE OF SOME PATIENTS WITH CARCINOID TUMORS,

21 PARTICULARLY CARCINOID TUMORS.

22 Q. IS THIS SOMETHING THAT'S FREQUENTLY MEASURED

23 IN PATIENTS WITH CARCINOID TUMORS?

24 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.

25 BY MS. WALTERS:

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1 Q. 5-HTP, I'M TALKING ABOUT.

2 MR. SIRRIDGE: MEASURED BY WHOM?

3 THE WITNESS: MEASURED BY WHOM?

4 BY MS. WALTERS:

5 Q. BY ANYONE YOU KNOW.

6 A. IS IT FREQUENTLY MEASURED IN PATIENTS

7 WITH --

8 Q. CARCINOID TUMORS.

9 A. I WOULD SAY OVERALL AS FAR AS IN HOSPITALS,

10 IT IS NOT FREQUENTLY MEASURED BECAUSE THE

11 MEASUREMENT IS NOT READILY AVAILABLE TO PEOPLE

12 THAT WOULD LIKE TO MEASURE IT. AND SO THAT LIMITS

13 THE AMOUNT THAT IT'S MEASURED BECAUSE IT'S A

14 SOPHISTICATED MEASUREMENT THAT'S NOT READILY

15 AVAILABLE, ALTHOUGH VERY USEFUL WHEN IT CAN BE

16 OBTAINED.

17 Q. HAS AN ELEVATED LEVEL OF 5-HTP EVER BEEN

18 FOUND TO YOUR KNOWLEDGE IN SMALL CELL LUNG TUMORS

19 OF THE LUNG?

20 A. I THINK THERE ARE PROBABLY -- SAY THE

21 QUESTION TO ME AGAIN.

22 (DESIGNATED QUESTION IS READ)

23 THE WITNESS: TO MY KNOWLEDGE, IT HAS

24 NOT BEEN FOUND IN SMALL CELL LUNG TUMORS IN THE

25 LUNG TUMORS TO MY KNOWLEDGE. I HAVE NOT SEEN A

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1 STUDY THAT PURPORTED TO SHOW THAT.

2 BY MS. WALTERS:

3 Q. WHEN YOU SAY IN THE TUMORS, WHAT DO YOU

4 MEAN? DOES YOUR RESPONSE INFER THAT THEY'VE BEEN

5 FOUND, HTP HAS BEEN FOUND SOMEPLACE OTHER THAN THE

6 TUMOR?

7 A. IT'S POSSIBLE IT COULD BE FOUND IN OTHER

8 PLACES THAN THE TUMOR.

9 Q. WHERE ELSE COULD IT BE FOUND?

10 A. WELL, ALTHOUGH I DON'T HAVE A PRECISE

11 RECOLLECTION THERE, I BELIEVE THERE ARE REPORTS OF

12 IT ON RARE OCCASIONS WHEN IT WAS MEASURED IN

13 REPORTS OF THE MEDICAL LITERATURE THAT IT WAS SAID

14 TO BE FOUND IN THE URINE IN ELEVATED AMOUNTS OF

15 SOME RARE PATIENTS WITH TUMORS OF THE LUNG. BUT

16 I --

17 Q. WHAT TYPE OF LUNG TUMORS?

18 A. I CAN'T RECALL THE PRECISE KIND OF LUNG

19 TUMORS THAT WAS SAID TO BE FOUND IN. THESE

20 REPORTS PROBABLY GO BACK TEN OR FIFTEEN YEARS AND

21 I JUST CAN'T PRECISELY ANSWER THAT, ANSWER THAT

22 QUESTION. POSSIBLY IN THE BIBLIOGRAPHY IN ONE OF

23 MY EARLIER REPORTS, BUT I CAN'T OFF THE TOP OF MY

24 HEAD REMEMBER.

25 Q. IS IT EASIER TO MEASURE THE 5-HTP IN THE

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1 URINE THAN IT WOULD BE TO MEASURE IT IN THE TUMOR
2 ITSELF?
3 A. YES. I WOULD SAY IT'S EASIER TO MEASURE IT
4 IN THE URINE.
5 Q. DO YOU KNOW WHETHER THERE HAVE BEEN ANY
6 PUBLISHED REPORTS OF 5-HTP BEING MEASURED IN
7 EITHER URINE OR THE TUMOR OF A SMALL CELL LUNG
8 CANCER PATIENT?
9 A. I THINK I ANSWERED THAT ONE, THAT I THOUGHT
10 THERE MIGHT BE, BUT I CAN'T RECALL A PRECISE
11 CITATION OR I CAN SAY FOR SURE WHAT TYPE OF TUMOR
12 IT WAS, WHETHER IT WAS SMALL CELL OR ADENOMA, I
13 JUST CAN'T REMEMBER THAT. I THINK THERE ARE
14 REPORTS IN THE EARLY STUDIES, PERHAPS TEN, TWELVE
15 YEARS AGO FROM ENGLAND, BUT I CAN'T REMEMBER
16 PRECISELY THE TUMOR. IT'S POSSIBLE IT'S IN SOME
17 OF MY REFERENCES OF MY BIBLIOGRAPHIES IN SOME OF
18 THE THINGS I'VE WRITTEN.
19 Q. IT'S POSSIBLE THAT SOME OF THOSE EARLIER
20 STUDIES SHOW AN INCREASED LEVEL OF 5-HTP IN LUNG
21 CANCER?
22 A. IT'S POSSIBLE IT IS AND IT'S POSSIBLE IT'S
23 NOT. I JUST CAN'T REMEMBER WITHOUT CONSULTING.
24 THAT'S THE PROBLEM, WITHOUT CONSULTING REFERENCES.
25 MR. NORTHRIP: DO YOU HAVE A

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1 REFERENCE YOU WANTED TO SHOW HIM, MISS WALTERS?

2 THE WITNESS: NO.

3 MR. NORTHRIP: MR. EDELL LIKES HIS

4 WITNESSES TO HAVE THE REFERENCE IN FRONT OF THEM

5 WHENEVER THEY ARE QUESTIOED ABOUT IT.

6 MS. WALTERS: I DON'T KNOW OF ANY

7 ARTICLE. I'M JUST ASKING THE DOCTOR IF HE KNOWS

8 OF ANY ARTICLE.

9 THE WITNESS: THERE MAY HAVE BEEN AN

10 ARTICLE A LONG TIME AGO.

11 MR. SIRRIDGE: THERE'S NO QUESTION

12 PENDING.

13 BY MS. WALTERS:

14 Q. DOCTOR, I THINK YOU INDICATED YOU DID NOT

15 GENERALLY MEASURE 5-HTP IN CARCINOID TUMORS. I'M

16 NOT SURE WHETHER WHEN I ASKED YOU THAT QUESTION

17 YOU WERE ALSO INCLUDING IN THAT RESPONSE WHETHER

18 YOU MEASURE 5-HTP IN URINE OF CARCINOID PATIENTS.

19 A. I HAVE IN THE PAST MEASURED 5-HTP IN URINE,

20 AND ON OCCASION, I HAVE TRIED TO MEASURE IN

21 TUMORS. THESE TUMORS TO MY RECOLLECTION HAVE ONLY

22 BEEN CARCINOID TUMORS THAT I'VE TRIED TO MEASURE

23 IN.

24 Q. WOULD THESE TUMORS BE LUNG TUMORS?

25 A. MY RECOLLECTION IS THAT THEY WERE NOT LUNG

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1 TUMORS, THAT THEY WERE STOMACH TUMORS OR ILEAL
2 TUMORS. I CAN'T REMEMBER LUNG TUMORS THAT I TRIED
3 TO MEASURE IN THE TUMOR.
4 Q. ARE YOU FAMILIAR WITH ANY LITERATURE IN
5 WHICH 5-HTP HAS BEEN MEASURED IN EITHER URINE OR
6 THE TUMOR ITSELF IN A BRONCHIAL CARCINOID?
7 A. YES, I'M FAMILIAR WITH THAT AND I THINK I
8 MYSELF HAVE MEASURED IN URINE OF THE PATIENTS WITH
9 BRONCHIAL CARCINOID. THE SAME CITATION OF THIS
10 REFERENCE, IF YOU WANT TO REFER TO IT.
11 Q. WHICH ARTICLE?
12 A. IT'S THE ARTICLE IN CLINICAL CHEMISTRY
13 CALLED -- IT'S REFERENCED 169 ON MY BIBLIOGRAPHY.
14 Q. IS THAT FROM CLINICAL CHEMISTRY?
15 A. CLINICAL CHEMISTRY.
16 Q. 1986?
17 A. YES. TABLE THREE, WHICH READS ON PAGE 843
18 OF THAT ARTICLE CITED, THE TITLE OF THE TABLE IS
19 RELATIONSHIP BETWEEN CLINICAL COURSE AND EXCRETION
20 OF 5-HTP AND ITS METABOLITES IN A PATIENT WITH A
21 BRONCHIAL CARCINOID TUMOR.
22 Q. SO IN THAT ONE TUMOR THAT'S DISCUSSED IN
23 TABLE THREE, YOU MEASURED 5-HTP; IS THAT CORRECT?
24 A. I'VE ALSO MEASURED -- I DIDN'T MEASURE THE
25 TUMOR.

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1 Q. YOU MEASURED IT IN THE URINE?

2 A. IN THE URINE OF THE PATIENT WITH THE

3 BRONCHIAL CARCINOID TUMOR.

4 Q. LET ME ASK YOU A QUESTION BEFORE YOU MOVE ON

5 JUST TO CLARIFY THAT. DOES 5-HTP IN THE TUMOR

6 HAVE TO BREAK DOWN BEFORE IT'S MEASURABLE IN THE

7 URINE?

8 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.

9 BY MS. WALTERS:

10 Q. IN OTHER WORDS, DOES IT TRAVEL FROM THE

11 TUMOR TO THE URINE BEFORE IT IS MEASURED,

12 MEASURABLE?

13 A. YES, YES. I WOULD SAY RATHER THAN SAY BREAK

14 DOWN, I WOULD SAY SECRETED BY THE TUMOR OR

15 RELEASED BY THE TUMOR AND IT GETS TO THE KIDNEYS

16 AND EXCRETED BY THE URINE AND THEN IT WOULD BE

17 MEASURED IN THE URINE.

18 Q. SO THE CONVERSION --

19 THE WITNESS: I SHOULD ADD --

20 MR. SIRRIDGE: THERE'S NO QUESTION

21 PENDING.

22 THE WITNESS: RIGHT.

23 BY MS. WALTERS:

24 Q. SO THE CONVERSION OF TRYPTOPHAN TO 5-HTP

25 OCCURS IN THE TUMOR; IS THAT CORRECT?

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1 MR. SIRRIDGE: COULD YOU READ THAT
2 BACK?
3 (DESIGNATED QUESTION IS READ)
4 THE WITNESS: THAT'S CORRECT.
5 BY MS. WALTERS:
6 Q. AND THEN SOME OF THAT 5-HTP COULD TRAVEL TO
7 THE URINE DIRECTLY; IS THAT CORRECT?
8 A. BY WAY OF THE KIDNEYS, BY WAY OF THE KIDNEYS
9 WHICH IS EXCRETED INTO THE URINE, THAT WOULD BE
10 CORRECT.
11 Q. SO THE TRYPTOPHAN MUST BE CONVERTED TO 5-HTP
12 IN THE TUMOR BEFORE IT CAN TRAVEL THROUGH THE
13 KIDNEY TO THE URINE AND BE MEASURABLE?
14 A. I WOULD SAY THAT'S ESSENTIALLY CORRECT, YES.
15 Q. HAVE YOU EVER MEASURED -- I'M SORRY. THE
16 5-HTP THAT WAS MEASURED IN THIS SINGLE CASE OF
17 BRONCHIAL CARCINOID IN THE 1986 ARTICLE -- CAN YOU
18 READ THAT BACK?
19 (DESIGNATED QUESTION IS READ)
20 MS. WALTERS: I'LL START OVER AGAIN
21 ANYWAY.
22 BY MS. WALTERS:
23 Q. HOW WAS THE 5-HTP MEASURED IN THE SINGLE
24 PATIENT WITH A BRONCHIAL CARCINOID TUMOR IN THE
25 1986 ARTICLE THAT WE'RE DISCUSSING, IS THAT URINE

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1 OR TUMOR MEASUREMENT?

2 (OBJECTION) MR. SIRRIDGE: I OBJECT TO THE FORM.

3 YOU'RE JUST TALKING ABOUT THE SINGLE PATIENT NOTED

4 IN TABLE THREE?

5 MS. WALTERS: CORRECT.

6 THE WITNESS: THAT WAS MEASURED IN

7 THE URINE BECAUSE IT SAYS EXCRETION OF 5-HTP.

8 BY MS. WALTERS:

9 Q. WERE THERE ANY OTHER BRONCHIAL CARCINOID

10 TUMORS THAT WERE MEASURED FOR 5-HTP?

11 A. YES, THERE WERE.

12 Q. IN THIS PARTICULAR ARTICLE?

13 A. YES.

14 Q. HOW MANY OTHERS WERE THERE?

15 A. IT WAS MEASURED ON PAGE 842 IN THE LAST

16 PARAGRAPH, I DESCRIBED MEASURING IT IN 26 OF 75

17 PATIENTS WITH CARCINOID TUMORS.

18 Q. HOW MANY OF THOSE WERE BRONCHIAL CARCINOIDS?

19 A. ORIGINALLY, ORIGINALLY THERE WAS A FIGURE

20 THAT CONTAINED THAT DATA, BUT FOR BREVITY, THE

21 EDITOR WANTED IT REMOVED, A FIGURE OR A TABLE

22 WHICH ACTUALLY TOLD HOW MANY WERE BRONCHIAL

23 CARCINOIDS, AND I CAN'T IMMEDIATELY RECALL HOW

24 MANY OF THE 26 OF THE SUBSTANTIAL NUMBER WERE

25 FORE-GUT, F-O-R-E HYPHEN G-U-T, OR CARCINOIDS.

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1 SOME OF THOSE ORIGINATED FROM THE BRONCHUS BUT I
2 CAN'T RECALL PRECISELY HOW MANY BECAUSE THE
3 ORIGINAL BREAKDOWN, THE DATA WAS REMOVED.
4 Q. WHAT WAS THE TOTAL NUMBER OF BRONCHIAL
5 CARCINOIDS IN THIS STUDY?
6 A. THERE WERE EIGHT PATIENTS WITH BRONCHIAL
7 CARCINOIDS THAT I OBTAINED A NUMBER FROM FIGURE
8 ONE, THE NUMBER OF DOTS OF BRONCHIAL CARCINOIDS.
9 SOME OF THOSE, IN ADDITION TO THE ONE I BELIEVE,
10 WE DID MEASURE 5-HYDROXYTRYPTOPHAN.
11 Q. I'M SORRY. COULD YOU READ THAT BACK?
12 A. THERE WERE EIGHT PATIENTS --
13 (DESIGNATED ANSWER IS READ)
14 BY MS. WALTERS:
15 Q. I DIDN'T UNDERSTAND YOUR RESPONSE. HOW MANY
16 OF THE EIGHT BRONCHIAL CARCINOIDS IN THE STUDY DID
17 YOU MEASURE THE 5-HTP IN?
18 MR. SIRRIDGE: HE ALREADY ANSWERED
19 THAT.
20 MS. WALTERS: I DIDN'T UNDERSTAND.
21 THAT'S WHY I ASKED AGAIN.
22 THE WITNESS: THE ORIGINAL WAY THE
23 PAPER WAS WRITTEN, MY RECOLLECTION IS THERE WAS A
24 TABLE THAT ACTUALLY SHOWED WHERE THE TUMOR
25 ORIGINATED AND WHAT THE MEASUREMENTS WERE BUT THE

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1 EDITOR ASKED ME TO REMOVE THE TABLE FROM THE PAPER
2 AND JUST STATE IT IN A PARAGRAPH. AND IN DOING
3 THIS FOR BREVITY, IT DOESN'T BREAK DOWN -- THERE'S
4 NOT A BREAKDOWN OF HOW MANY PATIENTS WERE
5 BRONCHIAL CARCINOID. AND FROM MY MEMORY BECAUSE I
6 JUST CAN'T RECALL THE EXACT NUMBER, BUT WE
7 MEASURED IN A TOTAL OF 26 OF THE 75 TOTAL
8 PATIENTS, 26 OF THE 75, AND OF THOSE 26, A CERTAIN
9 NUMBER WERE BRONCHIAL CARCINOIDS BUT I CAN'T COME
10 UP WITH THAT NUMBER RIGHT NOW.
11 BY MS. WALTERS:
12 Q. WELL, OF THE 26, EIGHT WERE BRONCHIAL
13 CARCINOIDS?
14 A. YES. BUT, SEE, OF THE 75, EIGHT WERE
15 BRONCHIAL CARCINOIDS.
16 Q. I'M SORRY. CORRECT.
17 A. SEE, THAT'S THE TOTAL NUMBER OF PATIENTS.
18 Q. BUT YOU DON'T KNOW HOW MANY OF THE 26 THAT
19 YOU MEASURED HTP IN WERE CARCINOIDS OF THE
20 BRONCHUS?
21 A. I DON'T KNOW RIGHT NOW. THE WAY THE DATA IS
22 IN THIS PAPER, I DON'T KNOW.
23 Q. DO YOU HAVE THAT INFORMATION SOMEWHERE ELSE?
24 A. I COULD FIND THAT INFORMATION, YES.
25 Q. (REQUEST) COULD YOU GIVE THAT TO MR.

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1 SIRRIDGE AND HE COULD FORWARD THAT TO ME?

2 MR. SIRRIDGE: YOU CAN MAKE A PROPER

3 REQUEST FOR IT OR ARE YOU REQUESTING IT NOW?

4 MS. WALTERS: I WOULD LIKE TO REQUEST

5 IT NOW. IS THAT PERMISSIBLE?

6 MR. SIRRIDGE: YES. WE WILL SEE IF

7 HE CAN FIND IT AND LOCATE IT.

8 MS. WALTERS: THANK YOU.

9 THE WITNESS: I WILL SEE IF I CAN

10 FIND IT.

11 MR. NORTHRIP: CAN I GET THE

12 INFORMATION FROM DR. SCHUMAN THAT MR. EDELL HAD

13 ASKED ME TO REQUEST IN WRITING?

14 MS. WALTERS: PLEASE. YOU HAVE TO

15 ADD ANOTHER MINUTE ONTO THE DEPOSITION TODAY.

16 MR. SIRRIDGE: OFF THE RECORD.

17 (OFF-THE-RECORD DISCUSSION)

18 BY MS. WALTERS:

19 Q. DOCTOR, HAVE YOU MEASURED 5-HTP IN ANY OTHER

20 BRONCHIAL CARCINOIDS IN OTHER THAN THE TUMORS THAT

21 WE'VE JUST DISCUSSED IN THIS 1986 PAPER?

22 MR. SIRRIDGE: I THINK THAT'S BEEN

23 ASKED AND ANSWERED.

24 THE WITNESS: CAN I ANSWER THAT?

25 MR. SIRRIDGE: WHY DON'T YOU REPEAT

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1 THE QUESTION?

2 THE WITNESS: REPEAT THE QUESTION.

3 MS. WALTERS: CAN YOU READ THAT BACK?

4 (DESIGNATED QUESTION IS READ)

5 THE WITNESS: THERE'S ONE OTHER --

6 THERE'S ONE OTHER PAPER FROM ABOUT EIGHT YEARS AGO

7 WHERE I DID MEASURE 5-HTP IN SOME PATIENTS.

8 BY MS. WALTERS:

9 Q. WERE THOSE BRONCHIAL CARCINOIDS?

10 A. I KNOW ONE WAS A GASTRIC CARCINOID. I

11 CANNOT RECALL IF THERE ARE BRONCHIAL CARCINOIDS.

12 IF YOU LOOK UP --

13 Q. WHAT PAPER IS IT? GIVE ME THE YEAR FIRST.

14 A. THE PAPER IS A PAPER PUBLISHED IN

15 GASTROENTEROLOGY UNDER THE QUESTION IS THE PAPER

16 PUBLISHED IN GASTROENTEROLOGY, 1978. IT'S VOLUME

17 75, PAGE 1109, 1978, CALLED SEROTONIN METABOLISM

18 IN PATIENTS WITH CARCINOID TUMORS: INCIDENCE OF

19 5-HYDROXYTRYPTOPHAN-SECRETING TUMORS. AND LOOKING

20 AT PAGE 1111 OF THAT PAPER, THERE'S A TABLE

21 SEROTONIN AND ITS METABOLITES IN PATIENTS WITH

22 TYPICAL CARCINOID TUMORS AND THE CARCINOID

23 SYNDROME. AND THE SECOND TABLE IS TABLE TWO,

24 SEROTONIN AND ITS METABOLITES IN PATIENTS WITH

25 ATYPICAL CARCINOID TUMORS. IN LOOKING AT THOSE

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1 TABLES, PATIENTS THREE AND SIX.

2 Q. AND 13?

3 A. 13.

4 Q. AND 21?

5 A. AND 21 HAD TUMORS ORIGINATING FROM THE

6 BRONCHUS, AND I DID MEASURE 5-HYDROXYTRYPTOPHAN IN

7 THOSE PATIENTS.

8 Q. OF THOSE FOUR TUMORS, HOW MANY WERE

9 ELEVATED? I THINK THE NORMAL IS AT THE BOTTOM?

10 A. RIGHT. I HAVE NOT LOOKED AT THIS FOR A

11 LITTLE WHILE.

12 Q. LET'S START WITH NUMBER THREE. NUMBER THREE

13 IS ELEVATED; IS THAT CORRECT?

14 A. NUMBER THREE IS 183, YES. NUMBER THREE IS

15 ELEVATED. OVER 50 WITH THAT METHOD OF MEASURING

16 WAS ELEVATED. THAT WAS A DIFFERENT METHOD OF

17 MEASURING THAN IN THE LATER PAPER ALTHOUGH THE

18 RANGE OF NORMAL IS SOMEWHAT ABOUT SIMILAR.

19 PATIENT SIX IS ELEVATED TO 1056. PATIENT 13 IS

20 ELEVATED 1811. PATIENT 21 IS ELEVATED WITH 833.

21 Q. SO ALL FOUR OF THESE WERE ELEVATED?

22 A. ALL FOUR WERE ELEVATED ON THAT PAPER.

23 Q. AND THEY'RE ALL URINARY EXCRETION?

24 A. THAT WAS URINARY EXCRETION OF 5-HTP. AND IN

25 THE SECOND TABLE WITH PEOPLE THAT HAD CLASSICAL

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1 ATYPICAL CARCINOID TUMORS, NONE OF THOSE WERE
2 KNOWN TO BE OF THE BRONCHUS.
3 Q. DOCTOR, ATYPICAL CARCINOID TUMOR, AS YOU USE
4 IT, IS NOT THE SAME THING AS AN ATYPICAL CARCINOID
5 THAT A PATHOLOGIST REFERS TO, IS IT?
6 A. WELL, IN MY WORK, I HAVE TO USE IT IN TWO
7 DIFFERENT WAYS. I HAVE TO UNDERSTAND WHAT THE
8 PATHOLOGIST IS CALLING AN ATYPICAL CARCINOID AND
9 THEY BASE THAT ON THE HISTOLOGICAL APPEARANCE OF
10 THE TUMOR UNDER THE MICROSCOPE. A SECOND WAY, AND
11 I ORIGINATED NEITHER OF THESE WAYS, A SECOND WAY
12 OF CALLING ATYPICAL IS CARCINOIDS THAT SECRETE
13 PREDOMINANTLY 5-HYDROXYTRYPTOPHAN RATHER THAN
14 SEROTONIN AND, IN FACT, ORIGINALLY WERE THOUGHT
15 NOT TO BE ABLE TO SECRETE VIRTUALLY ANY SEROTONIN.
16 Q. 5-HYDROXYTRYPTOPHAN IS 5-HT?
17 A. 5-HTP.
18 Q. HTP?
19 A. YES. AND THAT WAS ANOTHER WAY A TERM
20 STARTED QUITE INDEPENDENTLY FROM AUTHORS EITHER IN
21 ENGLAND OR THE NATIONAL INSTITUTE OF HEALTH. AND
22 THAT WAS THE SENSE IN WHICH I WAS USING IT IN THE
23 TABLE IN THE PAPER IN GASTROENTEROLOGY AS
24 REFLECTING THE ABILITY TO SECRETE EITHER SEROTONIN
25 OR 5-HYDROXYTRYPTOPHAN AND NOT REFERRING TO THE

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1 HISTOLOGICAL APPEARANCE.

2 Q. NOW, 5-HTP IS NOT THE SAME THING AS

3 SEROTONIN, IS IT?

4 A. NO, IT'S NOT.

5 Q. SEROTONIN IS A FURTHER -- IS SEROTONIN A

6 BREAKDOWN OF 5-HTP?

7 A. SEROTONIN, I WOULD CALL IT A METABOLITE OF

8 5-HTP IN THAT IT'S NOT AN END PRODUCT. I USUALLY

9 CALL BREAKDOWN THE FINAL END PRODUCT SO IT'S SORT

10 OF AN INTERMEDIATE OR METABOLITE OF IT.

11 Q. SO 5-HTP CONVERTS INTO SEROTONIN OR 5-HT, AS

12 WE'VE BEEN CALLING IT HERE, THROUGH WHAT PROCESS?

13 A. IT CONVERTS INTO IT BY AN ENZYME THAT WE

14 REFERRED TO EARLIER AND WE SAID WE'D ABBREVIATE IT

15 AS DOPA DECARBOXYLASE.

16 Q. AND IT CAN BREAK DOWN INTO IT -- STRIKE

17 THAT.

18 CAN 5-HTP BREAK DOWN INTO SEROTONIN IN THE

19 TUMOR ITSELF?

20 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.

21 BY MS. WALTERS:

22 Q. LET ME REPHRASE IT. I DON'T KNOW IF I USED

23 THE RIGHT LETTERS. DOES 5-HTP BREAK DOWN INTO

24 5-HT OR SEROTONIN IN THE TUMOR ITSELF?

25 A. YES, IT CAN. IT CAN.

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1 Q. AND CAN IT ALSO DO THAT IN THE URINE?
2 (OBJECTION) MR. SIRRIDGE: AGAIN, I OBJECT TO THE
3 FORM OF THE QUESTION.
4 THE WITNESS: WELL, IT CAN'T DO IT IN
5 THE URINE, BUT IT CAN DO IT IN OTHER TISSUES IN
6 THE BODY AND THEN BE EXCRETED IN THE URINE, BUT
7 IT'S NOT ACTUALLY IN THE URINE, IT WOULD NOT
8 OCCUR. IT NEEDS AN ENZYME TO CHANGE IT AND
9 THERE'S NOT AN ENZYME IN THE URINE.
10 BY MS. WALTERS:
11 Q. DOES 5-HTP GO SOMEWHERE OTHER THAN IN THE
12 TUMOR ITSELF AND IN THE URINE?
13 A. YES, IT DOES.
14 Q. WHERE ELSE DOES IT GO?
15 A. 5-HTP WOULD BE SECRETED THROUGHOUT. WHEN I
16 SAY LEAVES A TUMOR, IT GOES THROUGHOUT WHEREVER
17 THE BLOOD SUPPLY, THE BLOOD IN THE BODY GOES, THE
18 5-HTP WOULD BE CARRIED.
19 Q. CAN 5-HTP BE MEASURED IN THE BLOOD?
20 A. 5-HTP CAN BE MEASURED IN THE BLOOD IF YOU
21 HAVE A CERTAIN TYPE OF ANALYTICAL PROCEDURE.
22 Q. IS THAT ALSO A DIFFICULT OR MORE SENSITIVE
23 PROCEDURE?
24 A. THAT'S --
25 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.

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1 BY MS. WALTERS:

2 Q. YOU MAY ANSWER.

3 A. DIFFICULT PROCEDURE? WELL --

4 MR. SIRRIDGE: WHY DON'T YOU READ THE

5 QUESTION BACK?

6 BY MS. WALTERS:

7 Q. IS THAT A DIFFICULT PROCEDURE? I DON'T WANT

8 TO KNOW HOW TO DO IT. I JUST WANT TO KNOW IF IT'S

9 DIFFICULT.

10 A. MEASUREMENT OF 5-HYDROXYTRYPTOPHAN IN THE

11 BLOOD?

12 Q. YES.

13 A. IF SOMEONE WAS REALLY SKILLED IN IT, IT

14 WOULDN'T BE THAT DIFFICULT, BUT FOR AN AVERAGE

15 CLINICAL LABORATORY, IT WOULD BE DIFFICULT.

16 Q. HAVE YOU EVER MEASURED 5-HTP IN THE BLOOD OF

17 ANY OF THE CARCINOIDS OF THE BRONCHUS THAT YOU

18 HAVE TREATED OR CONSULTED WITH?

19 A. I HAVE NEVER MEASURED 5-HYDROXYTRYPTOPHAN IN

20 THE BLOOD IN MY LABORATORY, AS I CAN RECALL, IN

21 ANY PATIENT. I NEVER HAVE DONE THAT PARTICULAR

22 ANALYSIS.

23 Q. HAVE YOU EVER HAD IT DONE FOR YOU?

24 A. NO.

25 Q. HAVE YOU READ ANY ARTICLES IN THE LITERATURE

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1 WHERE ANYBODY HAS MEASURED 5-HTP IN THE BLOOD?
2 A. YES, I HAVE.
3 Q. HAVE ANY OF THOSE BEEN ON CARCINOIDS OF THE
4 LUNG?
5 A. MY RECOLLECTION IS THAT THEY'VE BEEN ON
6 CARCINOIDS BUT I CAN'T -- SOME AT LEAST HAVE BEEN
7 ON CARCINOIDS, BUT I CAN'T SPECIFICALLY RECALL OFF
8 THE TOP OF MY HEAD IF THEY WERE ON CARCINOIDS OF
9 THE LUNG.
10 Q. HAVE YOU SEEN IN THE LITERATURE ANY CASES OF
11 SMALL CELL CANCER OF THE LUNG IN WHICH THEY HAVE
12 MEASURED 5-HTP IN THE BLOOD?
13 A. I CANNOT RECALL SEEING ANY STUDIES IN THE
14 LITERATURE WHERE THEY MEASURED IN THE BLOOD IN
15 SMALL CELL CARCINOMAS OF THE LUNG.
16 Q. SO WE HAVE 5-HTP IN THE TUMOR, IN THE URINE
17 OR IN THE BLOOD; IS THAT CORRECT?
18 A. TUMOR, URINE AND THE BLOOD, THAT'S CORRECT.
19 Q. THEN 5-HTP CAN BREAK DOWN INTO SEROTONIN OR
20 5-HT IN ANY OF THOSE LOCATIONS?
21 (OBJECTION) MR. SIRRIDGE: I'M GOING TO OBJECT TO
22 THE FORM OF THE QUESTION.
23 BY MS. WALTERS:
24 Q. IS THAT CORRECT?
25 A. IT CAN BREAK DOWN -- 5-HTP -- IF YOU WILL

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1 JUST SAY THE QUESTION AGAIN.

2 MS. WALTERS: I'LL SAY IT AGAIN.

3 BY MS. WALTERS:

4 Q. DOES 5-HTP BREAK DOWN OR METABOLIZE INTO

5 SEROTONIN OR HT IN ANY ONE OF THOSE LOCATIONS?

6 (OBJECTION) MR. SIRRIDGE: I'M GOING TO OBJECT TO

7 THE FORM OF THE QUESTION. DR. FELDMAN HAS NOT

8 EQUATED THE TERMS BREAK DOWN AND METABOLIZE AS

9 SYNONYMS.

10 MS. WALTERS: I BELIEVE HE EQUATED

11 THEM, BUT HE USES BREAKDOWN AS A FINAL END PRODUCT

12 AS OPPOSED TO METABOLIZE WHICH IS ONE OF THE

13 INTERMEDIATE STEPS.

14 MR. SIRRIDGE: BUT YOU USED THEM

15 INTERCHANGEABLY IN YOUR QUESTION AND THAT'S WHY

16 I'M OBJECTING TO THE FORM.

17 THE WITNESS: I WOULD NOT NORMALLY

18 CALL 5-HTP A -- I MEAN SEROTONIN A BREAKDOWN OF

19 5-HTP. I MIGHT CALL 5-HIAA A BREAKDOWN OF

20 SEROTONIN BECAUSE THAT'S THE END THING THAT'S

21 SECRETED. IT'S THE END OF THE LINE, AND THAT'S

22 SORT OF A COMMON WAY, I THINK, THAT PEOPLE

23 DESCRIBE IT. THE END PRODUCT SOMETIMES IS A

24 BREAKDOWN BUT THE INTERMEDIATES AS METABOLITES,

25 NO. SO COULD YOU REPHRASE IT?

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1 BY MS. WALTERS:

2 Q. DOES HTP THEN METABOLIZE TO SEROTONIN OR HT

3 IN ALL THREE LOCATIONS; THAT IS THE TUMOR, THE

4 URINE AND THE BLOOD?

5 A. NO, IT WOULD ONLY BE CHANGED IN THE TUMOR.

6 IT WOULDN'T BE CHANGED IN THE BLOOD. IT WOULDN'T

7 BE METABOLIZED IN THE BLOOD AND IT WOULD NOT BE

8 METABOLIZED IN THE URINE. IT HAS TO BE

9 METABOLIZED IN AN ENZYME IN SOME SORT OF A TISSUE.

10 Q. AND THAT ENZYME IS DOPA DECARBOXYLASE?

11 A. THAT IS CORRECT.

12 Q. AND IS DOPA DECARBOXYLASE FOUND IN NORMAL

13 TISSUE OF THE LUNG?

14 A. YES, IT IS FOUND IN NORMAL TISSUE OF THE

15 LUNG AS IT'S FOUND IN MANY NORMAL TISSUES,

16 ACTUALLY, DOPA DECARBOXYLASE IS.

17 Q. IS DOPA DECARBOXYLASE ALSO FOUND IN TUMORS

18 OF THE LUNG?

19 A. IT'S FOUND IN SOME TUMORS OF THE LUNG BUT

20 NOT ALL TUMORS OF THE LUNG.

21 Q. IS IT FOUND IN SOME CARCINOID TUMORS?

22 A. IT IS FOUND IN SOME CARCINOID TUMORS OF THE

23 LUNG.

24 Q. IS IT FOUND IN ALL CARCINOID TUMORS OF THE

25 LUNG?

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1 A. NO, IT IS NOT FOUND IN ALL CARCINOID TUMORS.
2 Q. IS IT FOUND IN SOME SMALL CELL CANCERS OF
3 THE LUNG?
4 A. IT HAS BEEN FOUND IN SOME SMALL CELL CANCERS
5 OF THE LUNG, USUALLY IN LOWER CONCENTRATIONS OR
6 LOWER ENZYME ACTIVITY THAN IT'S FOUND IN CARCINOID
7 TUMORS OF THE LUNG, BUT IT HAS BEEN FOUND IN SOME
8 BY A NUMBER OF INVESTIGATORS.
9 Q. HAS ANY INVESTIGATOR OR YOURSELF, FOR THAT
10 MATTER, FOUND A REASON WHY IT IS FOUND IN SOME
11 TUMORS AND NOT OTHERS?
12 A. NO, IT'S JUST AN OBSERVATION THAT IT'S FOUND
13 IN SOME AND NOT OTHERS. THERE'S NO REAL
14 EXPLANATION WHY THAT HAPPENS. JUST SOME TUMORS
15 LACK THE ACTIVITY. SOME HAVE A LOT AND SOME HAVE
16 A TINY AMOUNT.
17 Q. SO IF THE TUMOR DOES NOT HAVE DOPA
18 DECARBOXYLASE PRESENT, IT CANNOT METABOLIZE 5-HTP
19 TO 5-HT; IS THAT CORRECT?
20 A. THAT IS CORRECT. THAT'S CORRECT.
21 Q. AND IN SUCH TUMORS, THE ONLY EXCRETION THAT
22 WOULD BE MEASURABLE WOULD BE THE 5-HTP; IS THAT
23 CORRECT?
24 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM OF
25 THE QUESTION.

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1 THE WITNESS: THE WAY IT'S PHRASED,
2 IT'S NOT CLEAR WHAT'S EXCRETED AND SO FORTH. IT'S
3 NOT CLEAR WHAT'S GOING WHERE.
4 BY MS. WALTERS:
5 Q. IN TUMORS WHERE THERE IS NO DOPA
6 DECARBOXYLASE, ONE WOULD NOT FIND HT SEROTONIN?
7 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
8 BY MS. WALTERS:
9 Q. IS THAT CORRECT?
10 THE WITNESS: IN THE TUMOR?
11 MR. SIRRIDGE: IN THE TUMOR?
12 BY MS. WALTERS:
13 Q. ANYWHERE.
14 A. ANYWHERE, NO. THE QUESTION WOULD BE --
15 THAT'S NOT TRUE. YOU WOULDN'T FIND IT ANYWHERE.
16 IN OTHER WORDS, YOU WOULD FIND IT SOMEWHERE.
17 Q. WHERE WOULD YOU FIND IT OR WHERE COULD YOU
18 FIND IT?
19 A. YOU COULD FIND 5-HT IN THE URINE OF PATIENTS
20 THAT HAVE TUMORS THAT DO NOT HAVE DOPA
21 DECARBOXYLASE.
22 Q. HOW WOULD THE 5-HT BE PRODUCED IF THERE IS
23 NO DOPA DECARBOXYLASE?
24 A. HOW WOULD 5-HTP BE PRODUCED? YOU SAID 5-HT.
25 Q. I THOUGHT I SAID 5-HT. IT SHOULD READ

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1 5-HT.

2 THE WITNESS: COULD YOU READ IT BACK?

3 MS. WALTERS: WHY DON'T I JUST STATE

4 IT AGAIN. IT WOULD BE FASTER.

5 BY MS. WALTERS:

6 Q. HOW WOULD THE 5-HT BE PRODUCED IN THE URINE

7 IF THERE IS NO DOPA DECARBOXYLASE PRESENT?

8 A. IT WOULD BE PRODUCED BECAUSE THE 5-HTP WOULD

9 BE RELEASED FROM THE TUMOR. IT WOULD BE CARRIED

10 BY THE BLOOD STREAM TO ALL THE TISSUES OF THE

11 BODY, INCLUDING THE LIVER, THE KIDNEY, ET CETERA.

12 IT WOULD GET INTO THESE TISSUES AND THESE TISSUES

13 CONTAIN DOPA DECARBOXYLASE, LIVER, KIDNEY, G.I.

14 TRACT, PROBABLY ALSO SOME OF THE LUNG, AND THEN

15 THE 5-HTP WOULD BE DECARBOXYLATED TO SEROTONIN

16 WITHIN THESE TISSUES AND THE SEROTONIN COULD THEN

17 BE EXCRETED IN THE URINE. SO THAT'S HOW IT COULD

18 GET IN THE URINE.

19 Q. SO THE ONLY PLACE -- STRIKE THAT.

20 SO IT IS NOT CORRECT THAT THE ONLY PLACE

21 THAT 5-HTP CAN BE CONVERTED TO 5-HT IS IN THE

22 TUMOR ITSELF?

23 (OBJECTION) MR. SIRRIDGE: I OBJECT TO THE FORM

24 OF THE QUESTION.

25 THE WITNESS: COULD YOU REPHRASE IT?

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1 BY MS. WALTERS:

2 Q. IT IS NOT CORRECT THAT THE ONLY PLACE THAT

3 5-HTP CAN BE METABOLIZED TO 5-HT IS IN THE TUMOR?

4 A. IT'S NOT CORRECT --

5 Q. IS THAT RIGHT, IT'S INCORRECT?

6 MR. SIRRIDGE: WHY DON'T YOU READ THE

7 QUESTION ONE MORE TIME?

8 MS. WALTERS: LET ME JUST TRY AGAIN.

9 THE WITNESS: IT'S A

10 NEGATIVE-NEGATIVE OR --

11 BY MS. WALTERS:

12 Q. SO THERE ARE PLACES OTHER THAN THE TUMOR

13 ITSELF WHERE 5-HTP CAN BE METABOLIZED TO 5-HT?

14 A. THAT IS CORRECT. THERE ARE OTHER PLACES.

15 Q. HOWEVER, IF THE DOPA DECARBOXYLASE IS NOT

16 PRESENT IN THE TUMOR, THE 5-HTP CANNOT BE

17 CONVERTED TO 5-HT IN THE TUMOR?

18 A. THAT IS CORRECT OR ELSE THERE'S A VERY SMALL

19 AMOUNT. SOMETIMES PART OF IT CAN BE CONVERTED IN

20 THE TUMOR BUT NOT ALL OF IT. IT'S NOT PROBABLY AN

21 ABSOLUTE. SOME OF THE TUMORS HAVE A LITTLE BIT OF

22 THE ENZYME IN THE TUMOR BUT NOT ENOUGH TO CONVERT

23 IT ALL.

24 Q. DOCTOR, THE 5-HT OR SEROTONIN THEN CAN BE

25 FOUND IN THE TUMOR ITSELF, IN THE URINE AND IN THE

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1 BLOOD?

2 A. WHAT KIND OF TUMOR ARE WE TALKING ABOUT? IS

3 THIS THE ONE THAT'S DEFICIENT OR --

4 Q. LET'S TALK -- NO. IT WOULDN'T BE ONE THAT'S

5 DEFICIENT. IT'S JUST IN GENERAL.

6 A. SO CARCINOID TUMORS IN GENERAL, COULD IT BE

7 FOUND IN THE --

8 MR. DECKER: IN THE LUNG OR JUST IN

9 GENERAL?

10 BY MS. WALTERS:

11 Q. IN THE LUNG. IN CARCINOID TUMORS OF THE

12 LUNG -- STRIKE THAT.

13 IN PATIENTS WITH CARCINOID TUMORS OF THE

14 LUNG, SEROTONIN OR HT CAN BE FOUND EITHER IN THE

15 TUMOR ITSELF, IN THE URINE OR IN THE BLOOD?

16 A. THAT'S CORRECT, IN SOME PATIENTS WITH

17 CERTAIN CARCINOID TUMORS OF THE LUNG.

18 Q. AND THOSE CERTAIN CARCINOID TUMORS -- NO,

19 STRIKE THAT.

20 THE ATYPICAL CARCINOID PATIENT THAT YOU HAVE

21 DESCRIBED, YOU WOULD NOT FIND THE HT IN THE TUMOR

22 ITSELF?

23 A. THE CLASSICAL DESCRIPTION IS YOU WOULD NOT

24 FIND IT IN THE TUMOR ITSELF.

25 Q. BUT YOU MIGHT FIND IT IN THE URINE AND THE

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1 BLOOD?

2 A. THAT'S RIGHT, BUT MY OWN STUDIES HAVE

3 SUGGESTED THERE ARE GRADATIONS OF THIS ATYPICAL

4 WORK. THERE MAY BE A CERTAIN SMALLER AMOUNT IN

5 THE TUMOR THAT IS NOT NECESSARILY AN ALL OR

6 NOTHING. THERE MAY BE A LITTLE BIT OF THE DOPA

7 DECARBOXYLASE SO THERE MAY BE SOME IN THE TUMOR

8 BUT NOT AS MUCH AS A TUMOR THAT'S GOT ITS FULL

9 COMPLIMENT OF DOPA DECARBOXYLASE TO QUALIFY IT.

10 Q. ARE THERE OTHER WAYS TO MEASURE THE

11 SEROTONIN LEVEL IN THE TUMOR ITSELF?

12 MR. SIRRIDGE: COULD YOU REPEAT

13 THAT?

14 BY MS. WALTERS:

15 Q. ARE THERE WAYS TO MEASURE THE SEROTONIN

16 LEVEL IN THE TUMOR ITSELF?

17 A. YES, THERE ARE.

18 Q. AND THERE ARE WAYS TO MEASURE THE SEROTONIN

19 IN THE URINE?

20 A. THAT IS CORRECT.

21 Q. AND THERE ARE WAYS TO MEASURE IT IN THE

22 BLOOD?

23 A. YES.

24 Q. ARE THESE THREE TESTS SOMETHING THAT YOU DO

25 AS A MATTER OF COURSE ON YOUR CARCINOID PATIENTS,

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1 THAT IS CARCINOID PATIENTS OF THE LUNG?

2 MR. SIRRIDGE: COULD YOU READ THE

3 QUESTION BACK?

4 MS. WALTERS: LET ME JUST REPHRASE

5 IT. I THINK IT'S FASTER TO REPHRASE IT IF YOU'RE

6 UNCERTAIN.

7 BY MS. WALTERS:

8 Q. THESE THREE TESTS FOR SEROTONIN WHICH YOU'VE

9 DESCRIBED IN THE TUMOR, IN THE URINE AND IN THE

10 BLOOD, ARE ALL THREE OF THESE TESTS PERFORMED BY

11 YOU AS A MATTER OF COURSE IN YOUR CARCINOID

12 PATIENTS?

13 MR. DECKER: EACH PATIENT?

14 MS. WALTERS: YES.

15 THE WITNESS: IF I CAN OBTAIN A

16 SPECIMEN FROM THE PATIENT, I'LL MAKE AN ATTEMPT TO

17 OBTAIN THE SPECIMEN AND THEN I WILL MEASURE IT IN

18 EACH PATIENT ALL OF THOSE THINGS AT LEAST ONE

19 TIME, IF I CAN OBTAIN A SPECIMEN. BUT THERE ARE

20 SOME TIMES WHEN I'M NOT ABLE TO GET THE SPECIMEN

21 AND THEN, OF COURSE, I HAVEN'T DONE IT ABSOLUTELY

22 IN ALL THREE. BUT WHEN I CAN GET THE SPECIMEN, I

23 MAKE AN EFFORT TO DO ALL THREE.

24 BY MS. WALTERS:

25 Q. GOING BACK TO THE COMPUTER PRINT-OUT, WHICH

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1 IS MARKED AS EXHIBIT 3 HERE TODAY, WOULD THAT TELL
2 US THE NUMBER OF PATIENTS WITH CARCINOID TUMORS OF
3 THE LUNG IN WHICH YOU'VE MEASURED EACH OF THESE
4 THREE TYPES OF SEROTONIN LEVELS?
5 A. WELL, IT TELLS SOME OF THAT INFORMATION. ON
6 THE ONES THAT SAID HAD A MALIGNANT COURSE, IT
7 TELLS THE 5-HIAA, THE SEROTONIN OF THE URINE AND
8 THE SEROTONIN OF THE PLATELETS WHICH I MEASURE
9 INSTEAD OF THE SEROTONIN OF BLOOD. THEY ARE A
10 VERY COMPARABLE MEASUREMENT BUT, TECHNICALLY, I
11 LIKE TO DO THIS ONE BETTER ON THE PATIENTS WITH
12 THE MALIGNANT CARCINOID TUMORS. WHERE THERE'S A
13 BLANK SPACE UNDER ANY OF THOSE COLUMNS, THAT MEANS
14 THAT I WASN'T ABLE TO GET THE SPECIMEN TO MEASURE
15 IT.
16 NOW, IN THE CASE OF THE ONES THAT HAD A
17 BENIGN CLINICAL COURSE, I INCLUDE ON THE FIRST
18 PAGE THE 5-HIAA AND THE SEROTONIN IN THE URINE BUT
19 I DON'T HAVE ON THAT ONE THE SEROTONIN OF THE
20 PLATELETS FOR LACK OF SPACE. AND THE FACT IS THAT
21 MY RECOLLECTION IS ALMOST ALL OF THE SEROTONIN OF
22 THE PLATELETS ON THOSE PATIENTS WAS WITHIN NORMAL
23 SO IT DIDN'T CONTRIBUTE THAT MUCH INFORMATION AND
24 I DIDN'T HAVE ROOM SO I TRIED TO PUT SOMETHING
25 THAT SEEMED MORE IMPORTANT.

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1 Q. SO ON YOUR BENIGN BRONCHIAL CARCINOIDS,
2 ESSENTIALLY ALL OF THE URINARY SEROTONIN AS WELL
3 AS THE BLOOD SEROTONIN WAS WITHIN NORMAL LIMITS
4 WITH ONE EXCEPTION AND THAT WOULD BE NUMBER 31, IS
5 THAT CORRECT -- NOT NUMBER 31 BUT THE
6 ONE --
7 A. 31-MONTH DIAGNOSIS AT PRESENT.
8 Q. RIGHT.
9 A. YES, THAT IS CORRECT. THAT IS CORRECT.
10 Q. DID YOU MEASURE FOR SEROTONIN IN THE TUMOR
11 ITSELF IN ANY OF THESE BENIGN CARCINOID --
12 A. YES, I DID. I DID MEASURE WHENEVER I CAN
13 GET THE TUMOR.
14 Q. IS THAT INDICATED ON HERE?
15 A. I KNOW THERE'S AT LEAST -- ONE OF THE
16 PROBLEMS WITH GETTING THE TUMOR IS SOMETIMES THE
17 TUMOR IS REMOVED AND IT'S SMALL AND IT'S PLACED IN
18 FORMALIN. AND ONCE IT'S IN FORMALIN, I CAN'T
19 MEASURE IT. SO SOMETIMES I JUST DON'T HAVE THE
20 OPPORTUNITY TO MEASURE IT. BUT I KNOW THAT IN AT
21 LEAST TWO OF THESE PATIENTS IN THE LIST THAT HAD A
22 BENIGN COURSE, I DID MEASURE THE SEROTONIN IN THE
23 TUMOR.
24 Q. JUST TWO OF THESE?
25 A. THERE MAY BE MORE. I CAN RECALL TWO OF

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1 THEM. I CAN'T TELL YOU EXACTLY WHICH ONE, BUT TWO
2 OF THEM, ONE WAS FAIRLY RECENT AND ANOTHER ONE WAS
3 A VERY HIGH VALUE SO I REMEMBER IT. I CAN'T
4 RECALL HOW MANY I DID IT ON. THAT IS NOT
5 SOMETHING THAT I HAVE IN MY COMPUTER DATA BASE,
6 THE SEROTONIN CONTENT OF THE CARCINOID TUMORS,
7 BECAUSE OF LIMITED SPACE. TWO OF THOSE, I KNOW I
8 DID MEASURE IT OF.
9 Q. TWO OF THE BENIGN CARCINOIDS HAD AN ELEVATED
10 LEVEL OF SEROTONIN IN THE TUMOR ITSELF; IS THAT
11 CORRECT?
12 A. YES, YES, THAT'S CORRECT. TWO OF THEM HAD
13 AN ELEVATED LEVEL.
14 Q. WAS ONE OF THOSE THE NUMBER 31, THE FEMALE
15 WITH A TEN POINT TWO HIAA READING?
16 A. I THINK THAT IS ONE THAT WAS HIGH, YES. MY
17 RECOLLECTION IS THAT'S PROBABLY ONE THAT WAS HIGH.
18 Q. WITH RESPECT TO THE MALIGNANT BRONCHIAL
19 TUMORS, YOU MEASURED SEROTONIN IN THE URINE AND
20 SEROTONIN IN THE BLOOD IN SOME OF THESE TUMORS BUT
21 NOT ALL OF THEM; IS THAT CORRECT?
22 A. IN SOME OF THE PATIENTS, NOT IN THE TUMORS.
23 Q. I'M SORRY. SOME OF THE PATIENTS?
24 A. IN SOME OF THE PATIENTS. I MEASURED IT IN
25 SOME. THE ONES I DIDN'T MEASURE WOULD HAVE A

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1 BLANK SPACE. AND I MEASURED THE 5-HIAA IN EVERY
2 ONE. AND IN THE MAJORITY I MEASURED THE OTHER
3 THINGS, BUT THERE ARE A FEW WHERE I WASN'T ABLE TO
4 GET THE SPECIMEN.
5 Q. DID YOU MEASURE THE ELEVATION OF SEROTONIN
6 IN THE TUMOR IN ANY OF THESE MALIGNANT BRONCHIAL
7 TUMORS THAT YOU'VE DESCRIBED?
8 A. MY RECOLLECTION IS THAT I DID MEASURE IT IN
9 SOME OF THESE TUMORS, YES.
10 Q. DO YOU RECALL WHAT THE RESULTS WERE?
11 A. I CAN'T RECALL THE RESULTS OF THEM.
12 Q. DO YOU HAVE THAT INFORMATION AVAILABLE?
13 A. I COULD TRY AND FIND THAT INFORMATION. I
14 DON'T HAVE IT, OF COURSE, AVAILABLE HERE.
15 Q. (REQUEST) I WOULD REQUEST THAT YOU ALSO
16 PRODUCE THAT INFORMATION WITH THE OTHER
17 INFORMATION THAT YOU'RE GOING TO GIVE MR.
18 SIRRIDGE.
19 MR. SIRRIDGE: YOUR REQUEST IS
20 NOTED.
21 BY MS. WALTERS:
22 Q. DOCTOR, HAVE YOU EVER DONE ANY RESEARCH OR
23 INVESTIGATION REGARDING THE SEROTONIN OR HT LEVELS
24 IN SMALL CELL CANCERS OF THE LUNG?
25 A. SEROTONIN LEVELS WHERE, IN THE TUMOR, IN THE

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1 URINE?

2 Q. TUMOR, URINE OR BLOOD.

3 A. YES, I HAVE. I HAVE MADE SOME OBSERVATIONS

4 ON THAT.

5 Q. WERE THOSE THE OBSERVATIONS THAT WE'VE

6 ALREADY DISCUSSED HERE TODAY EARLIER IN THE

7 SEVERAL ARTICLES?

8 A. YES, THEY WERE MAINLY THE OBSERVATIONS WE

9 DISCUSSED. IN ADDITION, THERE WERE OTHER

10 MEASUREMENTS I MADE OF 5-HIAA, YOU KNOW --

11 Q. WE'RE NOT TALKING ABOUT 5-HIAA. WE'RE

12 TALKING ABOUT HT LEVELS IN THE TUMOR OR URINE OR

13 BLOOD.

14 A. I HAVE ON OCCASION MEASURED THE SEROTONIN

15 LEVELS IN OCCASIONAL SMALL CELL CARCINOMAS, IF

16 THAT WAS THE QUESTION YOU'RE INTERESTED IN.

17 Q. CORRECT.

18 A. I HAVE OCCASIONALLY MEASURED IT. I HAVE ON

19 OCCASION MEASURED IT.

20 Q. AND ARE THE FINDINGS REFLECTED IN THESE

21 ARTICLES THAT WE'VE DISCUSSED TODAY OR ARE THERE

22 ADDITIONAL FINDINGS?

23 A. THERE ARE PROBABLY SOME UNPUBLISHED

24 OBSERVATIONS. I CAN'T RECALL THAT THOSE

25 OBSERVATIONS HAVE BEEN PUBLISHED.

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1 Q. DO YOU KNOW WHAT THOSE OBSERVATIONS ARE?
2 A. MY RECOLLECTION IS THAT WHEN I MEASURED IT
3 IN SMALL CELL CARCINOMAS, AND THERE'S A LIMITED
4 NUMBER BECAUSE, GENERALLY, YOU CAN'T GET AN
5 ADEQUATE AMOUNT OF TISSUE, BUT MY RECOLLECTION IS
6 THAT WHEN I'VE MEASURED IT, THE LEVELS HAVE ALWAYS
7 BEEN OF SEROTONIN IN THE TUMOR VERY LOW, BELOW THE
8 SENSITIVITY OF MY MEASUREMENTS BUT, YOU KNOW, VERY
9 LOW.
10 Q. THAT'S SEROTONIN IN THE TUMOR?
11 A. IN THE SMALL CELL TUMOR ON THE OCCASIONS
12 WHEN I DID MEASURE IT.
13 Q. HAVE YOU EVER MEASURED IT IN THE URINE OR
14 THE BLOOD?
15 A. I MEASURED IT IN THE URINE AND THE BLOOD IN
16 THE CASES WE'VE TALKED ABOUT THIS MORNING.
17 Q. ANY OTHER CASES?
18 A. I MEASURED IT IN THE URINE PROBABLY IN SOME
19 OTHER CASES THAT WE MENTIONED I HAD DONE OVER THE
20 YEARS IN A RANDOM MANNER, THAT IS NOT IN AN
21 UNIFORM WAY OF GETTING EVERY PATIENT I WOULD
22 ENCOUNTER.
23 Q. AND DO YOU RECALL WHAT THE FINDINGS WERE IN
24 THOSE?
25 A. I CAN RECALL FROM MEMORY ONLY, AND I DON'T

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1 HAVE THIS, AGAIN, IN AN ORGANIZED DATA BASE OR
2 ANYTHING, I CAN RECALL FROM MEMORY ONLY SIX
3 PATIENTS WHO HAD SMALL CELL CARCINOMAS THAT HAD
4 ANY INDICATION THAT THERE WAS AN ELEVATION OF
5 EITHER 5-HIAA OR SEROTONIN IN THEIR URINE OR IN
6 THE PLATELETS WHEN OCCASIONALLY THAT WAS MEASURED.
7 Q. THESE ARE SIX PATIENTS OTHER THAN THE ONES
8 THAT ARE INCLUDED IN THESE ARTICLES?
9 A. NO. THOSE ARE FIVE PATIENTS IN THOSE
10 ARTICLES AND I CAN ONLY RECALL ONE OTHER PATIENT
11 IN ADDITION TO THOSE ARTICLES, A PATIENT FROM
12 PERHAPS SIX YEARS AGO BEFORE THOSE STUDIES WERE
13 DONE.
14 Q. HOW MANY SUCH PATIENTS WOULD YOU HAVE
15 MEASURED FOR HT IN THE URINE? I'M TALKING ASIDE
16 FROM THE ONES THAT ARE PUBLISHED IN THESE
17 ARTICLES.
18 (OBJECTION) MR. SIRRIDGE: I'M GOING TO OBJECT TO
19 THE FORM. I'M NOT SURE THAT THAT ANSWER DEALT
20 JUST WITH HT IN THE URINE.
21 MS. WALTERS: IT DIDN'T. I'M
22 BREAKING IT DOWN.
23 THE WITNESS: SO NOW YOUR QUESTION IS
24 HOW MANY PATIENTS WITH SMALL CELL CARCINOMA --
25 MR. NORTHRIP: LET'S HEAR THE

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1 QUESTION AGAIN.

2 BY MS. WALTERS:

3 Q. HOW MANY PATIENTS WITH SMALL CELL CARCINOMA

4 OF THE LUNG HAVE YOU MEASURED FOR HT IN THE URINE

5 OTHER THAN THE ONES THAT ARE REFLECTED IN THESE

6 PUBLICATIONS WE'VE DISCUSSED TODAY?

7 A. I WOULD ESTIMATE IN THE PUBLICATIONS

8 DISCUSSED TODAY, THERE WERE 27, AND I WOULD

9 ESTIMATE THAT I MEASURED A TOTAL OF A HUNDRED. SO

10 I WOULD ESTIMATE FROM MY MEMORY THAT THERE WERE,

11 YOU KNOW, APPROXIMATELY 73 MORE TO MAKE A TOTAL OF

12 A HUNDRED WHICH IS A --

13 Q. SMALL CELL CANCERS OF THE LUNG?

14 A. SMALL CELL CANCERS OF THE LUNG, THAT I'VE

15 MEASURED IN THE ENTIRE TIME I'M MEASURING THEM, IN

16 17 YEARS, I WOULD ESTIMATE THAT I MUST HAVE

17 MEASURED APPROXIMATELY A HUNDRED.

18 Q. AND 73 ADDITIONAL TO THE ONES THAT ARE IN

19 THESE ARTICLES?

20 A. YES, APPROXIMATELY.

21 Q. AND OF THOSE 73, HOW MANY OF THEM -- I'M

22 SORRY. OF THOSE 73, HOW MANY DID YOU MEASURE FOR

23 HT IN THE URINE?

24 A. THAT I COULD NOT COME UP WITH A GOOD

25 ESTIMATE BECAUSE I'VE ALWAYS MEASURED 5-HIAA FROM

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1 THE DAY I STARTED BUT I HAVEN'T ALWAYS MEASURED
2 5-HT AND I'D HAVE TO SORT OF -- I COULDN'T REALLY
3 THINK. THERE WAS A PERIOD WHEN I MEASURED IT WITH
4 A METHOD I USED IN THIS PAPER AND THEN THERE WERE
5 TWO OR THREE YEARS WHEN I DIDN'T MEASURE IT. AND
6 THEN IN ABOUT '80, I STARTED MEASURING WITH A NEW
7 METHOD WHICH I'VE KEPT ON DOING UP UNTIL NOW. SO
8 I CAN'T SAY HOW MUCH I'VE MEASURED 5-HT ON. I CAN
9 ONLY RECALL THE 5-HIAA BECAUSE THAT WAS DONE
10 CONSISTENTLY FOR 17 YEARS.
11 Q. SO YOU ALSO COULDN'T RECALL HOW MANY OF
12 THOSE YOU TESTED FOR 5-HT IN THE BLOOD?
13 A. NO. THE SAME REASON I CAN'T RECALL THAT IS
14 BECAUSE THE BLOOD, AT ONE TIME I DID BLOOD -- I
15 DID SERUM SEROTONIN. THEN I STOPPED DOING ANY
16 BLOOD MEASURING FOR A YEAR OR TWO AND THEN I
17 STARTED DOING PLATELET SEROTONIN. AND NOW I DO
18 PLATELET AND SERUM SEROTONIN AGAIN WITH A NEW
19 METHOD. SO I JUST CAN'T, BECAUSE OF THE PERIODS
20 WHEN I DIDN'T MEASURE IT, I CAN'T COME UP WITH ANY
21 SORT OF USEFUL ESTIMATE.
22 Q. SO THE 73 SMALL CELL CANCERS OF THE LUNG
23 YOU'RE TALKING ABOUT ARE CASES THAT YOU MEASURED
24 FOR 5-HIAA?
25 A. YES, THAT I WOULD HAVE MEASURED AT LEAST

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1 5-HIAA, BUT MY RECOLLECTION IS AROUND A HUNDRED,
2 TOTAL OF A HUNDRED, MY RECOLLECTION.
3 Q. 73 ASIDE FROM THE ONES THAT ARE IN THESE
4 ARTICLES?
5 MR. SIRRIDGE: APPROXIMATELY.
6 THE WITNESS: APPROXIMATELY, YES,
7 APPROXIMATELY.
8 BY MS. WALTERS:
9 Q. WHAT YEAR DOES THAT DATE BACK TO?
10 A. IT WOULD DATE BACK TO -- STARTED IN 1970 AND
11 GO UNTIL 1987, 17-AND-A-HALF YEARS.
12 Q. 5-HIAA IS A BREAKDOWN OF SEROTONIN OR HT; IS
13 THAT CORRECT?
14 A. YES, THAT'S CORRECT.
15 Q. THAT'S THE FINAL END PRODUCT OF THIS LITTLE
16 PROCESS THAT WE'VE BEEN DISCUSSING HERE?
17 (OBJECTION) MR. SIRRIDGE: I WOULD OBJECT TO THE
18 FORM OF THAT.
19 THE WITNESS: YES.
20 BY MS. WALTERS:
21 Q. IT'S THE FINAL END PRODUCT OF THE PROCESS
22 THAT WE'VE BEEN DISCUSSING HERE TODAY; IS THAT
23 CORRECT?
24 A. THAT'S CORRECT.
25 Q. AND IS HT -- STRIKE THAT.

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1 IS 5-HIAA ALWAYS A BREAKDOWN OF SEROTONIN OR
2 CAN IT BE PRODUCED IN SOME OTHER FASHION?
3 A. 5-HIAA IS ALWAYS A BREAKDOWN OF SEROTONIN
4 AND I KNOW OF NO OTHER WAY IT CAN BE PRODUCED.
5 Q. CAN SEROTONIN BREAK DOWN INTO 5-HIAA IN THE
6 TUMOR ITSELF?
7 A. I WOULD SAY IT PROBABLY CAN IN THE TUMOR
8 ITSELF.
9 Q. CANNOT?
10 A. IT CAN. IT CAN BREAK DOWN IN THE TUMOR.
11 IT'S CAPABLE -- I DON'T KNOW WHAT THE MAGNITUDE OF
12 THAT IS, BUT THE ENZYME INVOLVED IN THE BREAKDOWN
13 IS FOUND IN THE TUMOR. THERE MAY BE
14 COMPARTMENTALIZATION BUT I WOULD SAY IT'S POSSIBLE
15 IT CAN.
16 Q. HAS IT EVER BEEN MEASURED IN THE TUMOR
17 ITSELF TO YOUR KNOWLEDGE, 5-HIAA?
18 A. YES, IT'S BEEN MEASURED BY SOME PEOPLE. NOT
19 BY ME. I HAVE NEVER TRIED TO MEASURE IT. I
20 DIDN'T FEEL THAT THE METHODS I HAD AVAILABLE TO ME
21 WERE SENSITIVE ENOUGH.
22 Q. AND DO YOU RECALL WHETHER THE PEOPLE THAT
23 HAVE MEASURED IT HAVE REPORTED IT OR PUBLISHED
24 THEIR CASES ON IT?
25 A. I THINK SOME OF THEM HAVE REPORTED CASES ON

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1 IT, 5-HIAA MEASUREMENTS, I THINK THEY HAVE.
2 Q. HAVE ANY OF THESE BEEN IN THE CARCINOIDS OF
3 THE LUNG?
4 A. I BELIEVE THEY HAVE. I BELIEVE SOME OF THEM
5 HAVE. I'M DOING THIS FROM MEMORY.
6 Q. HAVE ANY OF THEM BEEN IN SMALL CELL CANCERS
7 OF THE LUNG?
8 A. I'M NOT SURE ABOUT THAT. I'M NOT SURE IF
9 THEY HAVE BEEN IN SMALL CELLS. I CAN'T RECALL
10 THAT. PEOPLE WOULD MORE LIKELY DO THAT ON
11 CARCINOIDS OF THE LUNG, BUT I CAN'T SAY THAT --
12 Q. WHY IS THAT?
13 A. WELL, BECAUSE CARCINOIDS OF THE LUNG ARE
14 MORE ASSOCIATED WITH THE PRODUCTION OF SEROTONIN
15 AND 5-HIAA. AND IF PEOPLE WANTED TO TRY AND
16 MEASURE IT, THEY'D PROBABLY MEASURE IT IN A PLACE
17 WHERE IT WOULD BE MOST LIKELY TO OCCUR.
18 Q. HISTORICALLY HOW LONG HAS THE PRODUCTION OF
19 SEROTONIN AND 5-HIAA AND SO FORTH BEEN ASSOCIATED
20 WITH CARCINOID TUMORS?
21 A. SEROTONIN AND 5-HIAA HAVE BEEN ASSOCIATED
22 WITH CARCINOID TUMORS FOR APPROXIMATELY 25 YEARS
23 OR SO. I COULD FIND THAT PRECISE NUMBER BUT I
24 CAN'T FIND IT WITH THE THINGS I HAVE RIGHT HERE,
25 BUT IT WAS DESCRIBED ABOUT 25 YEARS AGO.

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1 Q. HOW LONG HAVE SEROTONIN AND 5-HIAA BEEN
2 ASSOCIATED WITH CARCINOID TUMORS OF THE LUNG?
3 A. OH, PROBABLY WITHIN TWO OR THREE YEARS OF
4 THE REPORT OF INITIALLY IT WAS CARCINOID TUMORS OF
5 THE ILEUM, SMALL INTESTINE, AND THERE WERE REPORTS
6 OF SEROTONIN PRODUCTION FROM CARCINOID TUMORS
7 ALONG WITH IT, I'D SAY, TWO OR THREE YEARS OF
8 THAT. WHATEVER NUMBER THAT IS, I'M JUST
9 ESTIMATING 25 YEARS. IT CERTAINLY IS IN THIS
10 CENTURY.
11 Q. WHEN WAS THE PRODUCTION OF SEROTONIN AND
12 5-HIAA FIRST ASSOCIATED IN THE LITERATURE TO YOUR
13 KNOWLEDGE WITH SMALL CELL TUMORS OF THE LUNG?
14 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM OF
15 THE QUESTION. IT'S ASSUMING THE PREVIOUS ANSWER.
16 BY MS. WALTERS:
17 Q. YOU CAN ANSWER THAT.
18 MR. SIRRIDGE: COULD YOU READ IT
19 BACK.
20 (DESIGNATED QUESTION IS READ)
21 THE WITNESS: I WOULD MAKE AN
22 ESTIMATE THAT IT WAS PROBABLY, IF IT WAS
23 ASSOCIATED OR MENTIONED IN ASSOCIATION WITH
24 BRONCHIAL CARCINOIDS THREE YEARS AFTER, THEN MAYBE
25 FOUR YEARS AFTER IT WAS FIRST DESCRIBED THERE WAS

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1 PROBABLY A REPORT MENTIONING IT, BUT I CAN'T TELL
2 YOU THE REPORT OFF THE TOP OF MY HEAD. I MEAN IT
3 GOES BACK A LITTLE WAY.
4 BY MS. WALTERS:
5 Q. APPROXIMATELY 21 YEARS?
6 MR. NORTHRIP: I THINK THAT MISLEADS
7 HIS TESTIMONY. I THOUGHT HE SAID 25 YEARS FOR
8 CARCINOIDS AND ABOUT THREE YEARS LATER FOR
9 BRONCHIAL.
10 THE WITNESS: BRONCHIALS, AND I'M
11 GUESSING THAT MAYBE FOUR YEARS AFTER FOR SMALL
12 CELL. BUT IT IS STRICTLY A SORT OF A MAGNITUDE
13 GUESS. IT'S IN THE RIGHT MAGNITUDE BUT --
14 BY MS. WALTERS:
15 Q. SO APPROXIMATELY 18 YEARS AGO?
16 MR. SIRRIDGE: APPROXIMATELY.
17 THE WITNESS: APPROXIMATELY, YES.
18 BUT WOULDN'T THAT BE 21 YEARS AGO? 25 YEARS AGO.
19 THEN MY ESTIMATE IS 22 YEARS AGO FOR CARCINOIDS,
20 BRONCHIAL CARCINOIDS, AND 21 YEARS AGO, THERE
21 MIGHT HAVE BEEN A REPORT ASSOCIATING SMALL CELL
22 CARCINOMA. I WOULD SAY, YOU KNOW, LIKE --
23 BY MS. WALTERS:
24 Q. 5-HIAA IS MORE FREQUENTLY MEASURED IN THE
25 URINE AND THE BLOOD; ISN'T THAT CORRECT?

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1 A. 5-HIAA IS MORE -- YES, THAT'S CORRECT. YOU
2 MEAN JUST IN GENERAL CLINICAL PRACTICE?
3 Q. YES, GENERAL.
4 A. THAT'S CORRECT.
5 Q. IS IT MORE FREQUENTLY MEASURED IN ONE THAN
6 THE OTHER?
7 A. WELL, I THINK I ANSWERED THAT.
8 Q. IS IT MORE FREQUENTLY MEASURED IN URINE THAN
9 IT IS IN BLOOD?
10 A. YES.
11 MR. SIRRIDGE: 5-HIAA?
12 BY MS. WALTERS:
13 Q. YES.
14 A. 5-HIAA IS MORE EFFECTIVELY MEASURED IN THE
15 URINE THAN IN THE BLOOD DEFINITELY.
16 Q. BUT IT'S MORE FREQUENTLY MEASURED IN THE
17 URINE AND BLOOD THAN OBVIOUSLY IN THE TUMOR
18 ITSELF?
19 A. IT'S RARELY MEASURED IN BLOOD.
20 Q. IT'S RARELY MEASURED IN BLOOD?
21 A. I THINK IT'S NOT OFTEN MEASURED IN BLOOD.
22 5-HIAA MEASURED IN BLOOD? SOME LABS DO IT, BUT I
23 KNOW IT'S NOT READILY COMMERCIALLY AVAILABLE IN
24 THE UNITED STATES THAT I KNOW OF.
25 Q. WHY IS IT RARELY TESTED IN BLOOD?

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1 A. WELL, BECAUSE AS SOON AS IT'S FORMED, IT'S
2 GOT A VERY LOW -- WHAT THEY CALL A VERY LOW RENAL
3 THRESHOLD, THAT IS THE KIDNEYS EXCRETE IT FROM THE
4 BLOOD AT A VERY, VERY LOW LEVEL FROM THE BLOOD, SO
5 IT NEVER BUILDS UP IN THE BLOOD TO A LEVEL WHERE
6 IN THE PAST PEOPLE COULD MEASURE IT WELL UNLESS
7 THEY HAD SOPHISTICATED EXPENSIVE EQUIPMENT.
8 Q. SO THE URINE IS THE BETTER PLACE TO MEASURE
9 IT?
10 A. YES, IT ENDS UP IN THE URINE AND IT'S THE
11 FINAL PLACE IT GOES SO IT ENDS UP IN A HIGH
12 CONCENTRATION, AND IT CAN BE MEASURED THERE.
13 MR. SIRRIDGE: WE'VE BEEN GOING FOR
14 ABOUT AN HOUR AND 25 MINUTES. WOULD THIS BE A
15 CONVENIENT TIME FOR A BREAK?
16 MS. WALTERS: TEN MINUTES.
17 (BRIEF RECESS)
18 BY MS. WALTERS:
19 Q. DOCTOR, DO SOME CARCINOIDS OF THE LUNG HAVE
20 ELEVATED 5-HTP IN THE TUMOR BUT NOT IN THE URINE
21 AND NOT IN THE BLOOD?
22 A. TO MY KNOWLEDGE, THEY DON'T. I DON'T KNOW
23 OF ANY THAT WOULD HAVE INCREASED 5-HTP IN THE
24 TUMOR BUT NOT IN THE BLOOD OR THE URINE.
25 Q. SO IN ANY TUMOR THAT HAS AN INCREASE IN THE

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1 5-HTP, YOU WOULD ALSO FIND IT IN THE URINE AND IN
2 THE BLOOD?
3 MR. SIRRIDGE: COULD YOU READ THAT
4 QUESTION BACK?
5 (DESIGNATED QUESTION IS READ)
6 (OBJECTION) MR. SIRRIDGE: OBJECT TO IT AS NON
7 SEQUITUR.
8 THE WITNESS: I WOULD SAY NOT
9 NECESSARILY. YOU WOULDN'T NECESSARILY FIND IT.
10 IT WOULD PROBABLY DEPEND ON EVEN, FOR INSTANCE,
11 THE SIZE OF THE TUMOR. IF THE TUMOR WAS VERY
12 TINY, IT COULD HAVE IT IN THERE BUT IT WOULDN'T BE
13 ENOUGH TO ELEVATE IT IN THE BLOOD AND NOT THE
14 URINE. SO IT WOULDN'T INEVITABLY -- IF THE TUMOR
15 WAS REAL SMALL, IT COULD HAVE IT IN THERE AND MAKE
16 IT, BUT IT'S SO SMALL EVEN WHEN IT RELEASES IT, IT
17 WOULDN'T BE RELEASING ENOUGH TO RAISE THE LEVELS
18 IN THE BLOOD AND THE URINE BECAUSE THE TUMOR IS
19 JUST TOO SMALL TO RAISE IT. IT NOT ONLY HAS TO
20 HAVE IT BUT IT USUALLY HAS TO BE A CERTAIN SIZE
21 PROBABLY.
22 BY MS. WALTERS:
23 Q. COULD A TUMOR SECRETE INTO THE URINE AND NOT
24 SECRETE INTO THE BLOOD? AND, AGAIN, I'M TALKING
25 ABOUT 5-HTP.

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1 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM OF
2 THE QUESTION.
3 THE WITNESS: IT COULDN'T SECRETE IN
4 THE URINE AND NOT IN THE BLOOD. THE CHEMICAL
5 MIGHT BE FOUND IN THE URINE AND NOT IN THE BLOOD.
6 BY MS. WALTERS:
7 Q. WHY WOULD THE CHEMICAL BE FOUND IN THE URINE
8 AND NOT IN THE BLOOD?
9 A. WELL, IT WOULD BE, FOR INSTANCE, LIKE 5-HIAA
10 IS EASILY FOUND IN THE URINE BUT NOT IN THE BLOOD
11 BECAUSE IT HAS WHAT WE CALL A LOW RENAL THRESHOLD
12 SO AS SOON AS IT GETS IN THE BLOOD, EVEN IN TINY
13 AMOUNTS TOO LOW TO MEASURE, IT'S EXCRETED INTO THE
14 URINE. SO IT MIGHT PASS THROUGH THE BLOOD BUT
15 IT'S NOT ENOUGH TO BE ABLE TO MEASURE IT BY, SAY,
16 THE METHODS IN USE AT THE TIME.
17 Q. SO YOU MIGHT HAVE AN INCREASE IN THE URINE
18 BUT NO INCREASE IN THE BLOOD?
19 A. YES.
20 Q. WOULD YOU EVER HAVE AN INCREASE IN THE BLOOD
21 WITH NO INCREASE IN THE URINE?
22 A. OF WHICH CHEMICAL?
23 Q. 5-HTP.
24 MR. SIRRIDGE: IN CARCINOID TUMORS --
25 MS. WALTERS: I'M TALKING ABOUT ANY

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1 TUMORS BECAUSE I THINK HE'S LIMITED HIS RESPONSE
2 TO WHAT PRODUCES THIS -- I MEAN I THINK WHAT
3 TUMORS PRODUCES HE'S ALREADY DESCRIBED EARLIER IN
4 THE DEPOSITION SO I'M NOT GOING TO TRY TO NARROW
5 IT. I'M JUST GOING TO SAY TUMORS IN GENERAL.
6 THE WITNESS: COULD YOU EVER FIND IT
7 IN THE BLOOD AND NOT IN THE URINE? I WOULD SAY
8 THE ONLY WAY THAT MIGHT OCCUR IS IF THE PATIENT
9 HAD SOME KIND OF KIDNEY DISEASE AND HE COULDN'T
10 EXCRETE IT IN THE URINE LIKE KIDNEY FAILURE OR
11 SOMETHING LIKE THAT. I WOULD THINK THAT IF IT GOT
12 IN THE BLOOD, IT COULD BE FOUND IN THE URINE IF
13 SOMEBODY HAD REASONABLY NORMAL KIDNEY FUNCTION.
14 BY MS. WALTERS:
15 Q. WHAT ABOUT 5-HT, COULD THAT BE ELEVATED IN
16 THE TUMOR BUT NOT ELEVATED IN THE URINE OR THE
17 BLOOD?
18 A. YES.
19 Q. WHEN WOULD THAT HAPPEN?
20 A. THAT WOULD HAPPEN IF, FOR INSTANCE, THE
21 TUMOR -- IT'S A LITTLE BIT LIKE THE ANSWER TO THE
22 QUESTION CAN 5-HYDROXYTRYPTOPHAN BE ELEVATED IN
23 THE TUMOR. THAT WOULD BE ONE EXAMPLE IF THE TUMOR
24 WAS REAL SMALL, LIKE IT WAS ONLY HALF A CENTIMETER
25 ACROSS SO IT CAN MAKE THE 5-HT AND SECRETE THE

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1 5-HT BUT CAN'T MAKE ENOUGH TO RAISE THE LEVEL IN
2 THE BLOOD AND URINE ABOVE NORMAL.
3 THE SECOND POSSIBILITY, ALTHOUGH THAT'S NOT
4 AS WELL-DOCUMENTED, IS THE TUMOR CAN MAKE THE
5 SEROTONIN AND STORES IT IN THE TUMOR, BUT FOR SOME
6 REASON, IT DOESN'T SECRETE IT AS MUCH. IN OTHER
7 WORDS, IT JUST KEEPS IT IN THERE. THAT'S ALSO
8 WITHIN THE REALM OF POSSIBILITY.
9 Q. ANY THEORIES ABOUT WHY IT WOULD DO THAT?
10 A. NO, I REALLY DON'T HAVE ANY THEORIES. YOU
11 MEAN ABOUT WHY IT WOULD STORE IT BUT NOT SECRETE
12 IT? NO, I DON'T, BUT THERE ARE SOME OTHER
13 PARALLELS IN OTHER TYPE OF ENDOCRINE TUMORS THAT
14 OCCASIONALLY THAT HAPPENS, BUT NO EXPLANATION.
15 IT'S JUST SORT OF AN OBSERVATION THAT IT HAPPENS,
16 IT CAN HAPPEN.
17 Q. COULD A TUMOR -- STRIKE THAT.
18 COULD 5-HT BE ELEVATED IN THE URINE BUT NOT
19 IN THE BLOOD?
20 A. YES, IT CAN.
21 Q. AND WHEN WOULD THAT HAPPEN?
22 A. THAT CAN HAPPEN, FOR INSTANCE, IT COULD
23 HAPPEN IF THE PATIENT IS TAKING A MEDICATION THAT
24 INTERFERES WITH THE STORAGE OF THE 5-HT IN THE
25 BLOOD PLATELETS. EXAMPLES ARE WITH RESERPINE OR

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1 TRICYCLIC, ANTIDEPRESSANTS, THEN THE PLATELETS
2 CAN'T STORE IT WELL SO IT'S NOT HIGH IN THE BLOOD
3 BUT IT GOES OUT IN THE URINE. ANOTHER WAY THAT
4 HAPPENS, THE SECOND COMMON WAY WOULD BE IF AN
5 INDIVIDUAL HAS A TUMOR THAT IS DEFICIENT IN THE
6 ENZYME DOPA DECARBOXYLASE. WHAT THIS WILL DO IS
7 SECRETE 5-HYDROXYTRYPTOPHAN FROM THE TUMOR. THE
8 5-HYDROXYTRYPTOPHAN IS NOT STORED IN THE
9 PLATELETS. IT GOES TO THE KIDNEY WHERE IT'S
10 CHANGED TO SEROTONIN AND THEN THE KIDNEY EXCRETES
11 IT IN THE URINE. SO A FAIRLY CHARACTERISTIC
12 FINDING IN THESE TUMORS THAT SECRETE
13 5-HYDROXYTRYPTOPHAN IS THAT THE BLOOD WILL BE
14 EITHER NORMAL OR THE BLOOD PLATELET, SEROTONIN
15 WILL BE NORMAL OR JUST MINIMALLY ELEVATED AND THE
16 URINARY SEROTONIN WILL BE QUITE HIGH.
17 Q. IS THIS THE TUMOR THAT WE DISCUSSED EARLIER
18 -- I MEAN -- STRIKE THAT.
19 IS THIS WHAT YOU DISCUSSED EARLIER AND
20 CHARACTERIZED AS AN ATYPICAL CARCINOID?
21 A. YES, THAT WOULD BE AN ATYPICAL CARCINOID.
22 ATYPICAL IN THE BIOCHEMICAL SENSE, NOT THE
23 HISTOLOGICAL.
24 Q. I MEAN IF A SMALL CELL TUMOR WERE TO PRODUCE
25 5-HTP IN THE TUMOR AND IT HAD NO DOPA

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1 DECARBOXYLASE -- WELL, I'M NOT GOING TO GO THROUGH
2 ALL THAT. LET ME JUST ASK THIS QUESTION.
3 IF THAT SERIES OF EVENTS OCCURRED IN A SMALL
4 CELL CANCER, WOULD THAT ALSO BE CALLED AN ATYPICAL
5 CARCINOID?
6 (OBJECTION) MR. SIRRIDGE: I'M GOING TO OBJECT TO
7 THE FORM OF THE QUESTION.
8 MS. WALTERS: GO AHEAD.
9 THE WITNESS: I CAN'T. IT'S NOT
10 CLEAR ENOUGH FOR ME TO ANSWER IT.
11 BY MS. WALTERS:
12 Q. HOW WOULD YOU DESCRIBE THAT SERIES OF EVENTS
13 IF IT OCCURRED IN A SMALL CELL CANCER, WHAT KIND
14 OF A LABEL WOULD YOU PLACE ON IT?
15 (OBJECTION) MR. SIRRIDGE: I'M STILL GOING TO
16 OBJECT TO THE FORM OF THE QUESTION.
17 BY MS. WALTERS:
18 Q. FROM A BIOCHEMICAL STANDPOINT.
19 A. I DON'T HAVE A GRASP FOR WHAT IT IS. IT'S A
20 SMALL CELL THAT DOES WHAT?
21 Q. THAT'S DEFICIENT IN DOPA DECARBOXYLASE THAT
22 SECRETES 5-HTP BUT IT IS NOT STORED AND THE
23 SEROTONIN IS EXCRETED IN THE URINE.
24 A. YOU KNOW, THERE ISN'T REALLY A WORD TO
25 DESCRIBE THAT BECAUSE IT'S SORT OF UNCOMMON SO I

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1 DON'T THINK THERE'S A WORD IN THE MEDICAL
2 LITERATURE TO DESCRIBE THAT. IT'S SO UNCOMMON FOR
3 A SMALL CELL CARCINOMA TO MAKE MUCH SEROTONIN THAT
4 IN THE LIKELY EVENT IT MADE IT AND IT DIDN'T HAVE
5 THE ENZYME TO CONVERT THE 5-HYDROXYTRYPTOPHAN, I
6 DON'T KNOW THAT THAT'S BEEN DESCRIBED AS SORT OF A
7 NAME PUT ON IT.
8 Q. HAVE THERE BEEN A SERIES OF CASES OF SMALL
9 CELL CARCINOMA OF THE LUNG IN THE LITERATURE THAT
10 TO YOUR KNOWLEDGE FIND A RATHER CONSISTENT OR MORE
11 FREQUENT ELEVATION OF SEROTONIN IN SMALL CELL
12 CANCER THAN WHAT YOU HAVE FOUND?
13 (OBJECTION) MR. SIRRIDGE: I'M GOING TO OBJECT TO
14 THE FORM OF THE QUESTION. COULD YOU READ IT BACK,
15 PLEASE?
16 (DESIGNATED QUESTION IS READ)
17 THE WITNESS: YOU MEAN -- I DON'T
18 UNDERSTAND HOW YOU WANT THE ELEVATION TO BE
19 MEASURED. IN OTHER WORDS, IS THIS MEASURING IT IN
20 THE URINE OR THE BLOOD OR THE TUMOR? SEE, THERE'S
21 DIFFERENT WAYS OF LOOKING AT THAT. I CAN'T --
22 IT'S HARD FOR ME TO ANSWER UNLESS I KNOW IF YOU
23 WANT ME -- ARE YOU ASKING ME ARE THERE OTHER
24 SERIES THAT MEASURED IT AND FOUND IT IN THE URINE
25 MORE FREQUENT THAN I HAVE?

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1 BY MS. WALTERS:

2 Q. ALL RIGHT. WE'LL START WITH THAT. ARE

3 THERE OTHER SERIES THAT HAVE MEASURED IT AND FOUND

4 IT IN THE URINE MORE FREQUENTLY THAN YOU HAVE?

5 A. I'M NOT AWARE OF ANY THAT HAVE FOUND IT MORE

6 FREQUENTLY THAN I HAVE.

7 Q. WE'RE TALKING THEN ABOUT HT?

8 A. WE'RE NOW TALKING ABOUT HT.

9 Q. AND 5-HIAA?

10 A. AND 5-HIAA. I'M NOT AWARE OF OTHER SERIES

11 THAT HAVE FOUND IT MORE FREQUENTLY THAN I HAVE IN

12 THE URINE.

13 Q. HOW ABOUT IN THE BLOOD?

14 A. I'M NOT AWARE OF OTHER SERIES THAT HAVE

15 FOUND IT MORE FREQUENTLY IN THE BLOOD THAN I HAVE,

16 5-HT. 5-HTP, I'M NOT AWARE OF STUDIES THAT HAVE

17 LOOKED AT IT IN THE BLOOD. THERE MAY BE BUT I'M

18 NOT AWARE OF.

19 Q. ARE YOU AWARE OF ANY STUDIES THAT HAVE

20 LOOKED AT 5-HTP IN THE URINE?

21 A. NOT IN SMALL CELL IN SIGNIFICANT NUMBERS.

22 I'M NOT AWARE OF IT IN SIGNIFICANT NUMBERS.

23 Q. ARE YOU AWARE OF ANY OTHER SERIES OF SMALL

24 CELL CANCERS OF THE LUNG THAT HAVE FOUND ELEVATED

25 SEROTONIN OR 5-HIAA IN THE TUMOR? WELL,

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1 OBVIOUSLY, 5-HIAA WOULD NOT BE IN THE TUMOR?
2 A. RIGHT. SEROTONIN IN THE TUMOR?
3 Q. YES.
4 A. THERE ARE SOME STUDIES THAT HAVE MEASURED IT
5 USING HISTOCHEMICAL METHODS. THAT IS THEY HAVE AN
6 ANTIBODY AGAINST SEROTONIN AND THEY MEASURE IN A
7 SEMI-QUANTITATIVE WAY, IF THE -- THEY EXPOSE THE
8 TISSUE TO THE ANTIBODY, AND THEY THEN SEE IF --
9 THEY DO SORT OF A COMPLICATED ENZYME
10 ANTIGEN-ANTIBODY REACTION AND SEE IF THERE'S ANY
11 STAINABLE SEROTONIN. NOW, SOME OF THOSE METHODS
12 HAVE LOOKED AT CARCINOID TUMORS AND FOUND THAT,
13 BUT I CAN'T SAY OFF THE TOP OF MY HEAD IF THEY'VE
14 LOOKED AT SMALL CELL TUMORS SPECIFICALLY FOR
15 SEROTONIN. I KNOW THEY'VE -- SOME OF THOSE HAVE
16 FOUND A HIGH PERCENTAGE OF CARCINOID TUMORS AND
17 THEY MAY HAVE AN INCIDENTAL FINDING LOOKED AT SOME
18 OAT CELL TUMORS BUT I'M NOT AWARE. I CAN'T BE
19 SURE ABOUT THAT IF THEY DID THAT, IF THEY INCLUDED
20 THAT IN THEIR STUDY. THIS IS USING THIS
21 HISTOCHEMICAL METHOD WHERE THEY DON'T, YOU KNOW --
22 Q. IN THE ATYPICAL CARCINOID THAT YOU JUST
23 DISCUSSED USING THAT IN A BIOCHEMICAL SENSE, THAT
24 OCCURS IN THE CASE WHERE YOU HAVE AN INCREASE OF
25 5-HT IN THE URINE BUT A NORMAL AMOUNT IN THE

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1 BLOOD; IS THAT CORRECT?
2 A. THAT FREQUENTLY -- FREQUENTLY, THEY HAVE A
3 GREATER PROPORTION IN THE URINE THAN IN THE BLOOD.
4 Q. WOULD YOU ALSO HAVE AN INCREASE OF 5-HIAA IN
5 THE URINE IN THAT PARTICULAR CASE?
6 A. YOU FREQUENTLY WILL HAVE SOME INCREASE IN
7 5-HIAA BUT IT WON'T BE AS HIGH AS YOU MIGHT
8 ANTICIPATE, AND, FREQUENTLY, I LOOKED AT THE
9 RELATIONSHIP BETWEEN THE 5-HIAA IN THE URINE AND
10 THE SEROTONIN IN THE URINE TO SEE THE RELATIONSHIP
11 BETWEEN THE TWO AND THE BIOCHEMICALLY -- IN THE
12 MORE BIOCHEMICAL SENSE, ATYPICAL TUMORS, THE
13 SEROTONIN PROPORTION WILL BE HIGHER IN
14 RELATIONSHIP TO ANY GIVEN VALUE OF THE 5-HIAA, BUT
15 THEY BOTH MAY BE ELEVATED.
16 Q. SO THE SEROTONIN LEVEL IN THE URINE WILL BE
17 MORE ELEVATED THAN THE 5-HIAA LEVEL IN THE URINE?
18 MR. SIRRIDGE: I'M SORRY. COULD YOU
19 REPEAT THAT?
20 (DESIGNATED QUESTION IS READ)
21 THE WITNESS: NOT NECESSARILY IN
22 ABSOLUTE TERMS, BUT IN RELATIVE TERMS IT WILL BE
23 MORE ELEVATED. IN MILLIGRAMS, IF YOU TOOK
24 MILLIGRAMS AND MICROGRAMS, IT MIGHT NOT BE. BUT
25 IF YOU LOOKED AT SORT OF THE RATIO BETWEEN THE

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1 TWO, IT WOULD BE MORE ELEVATED.

2 BY MS. WALTERS:

3 Q. AND IN THE ATYPICAL CARCINOID THAT WE'RE

4 DISCUSSING IN A BIOCHEMICAL SENSE, CAN YOU FIND AN

5 INCREASE IN THE SEROTONIN LEVEL IN THE URINE AND,

6 YET, HAVE A NORMAL 5-HIAA READING?

7 MR. SIRRIDGE: IN THE WHAT?

8 BY MS. WALTERS:

9 Q. IN THE URINE.

10 A. LET'S SEE. I'M SORRY. WOULD YOU SAY IT ONE

11 MORE TIME?

12 Q. IN THE ATYPICAL CARCINOID THAT WE'RE

13 DISCUSSING IN A BIOCHEMICAL SENSE, COULD YOU ALSO

14 FIND AN INCREASE IN THE SEROTONIN IN THE URINE AND

15 HAVE A NORMAL 5-HIAA READING IN THE URINE?

16 A. YOU COULD. YOU COULD HAVE THAT, BUT,

17 USUALLY, 90 PERCENT OF THE TIMES, THE 5-HIAA IS

18 ALSO ELEVATED. BUT NOT IN PROPORTION. AND I DEAL

19 WITH THAT IN THE CLINICAL CHEMISTRY PAPER WE

20 TALKED ABOUT, IF YOU WANT TO REFER TO THAT. IN

21 OTHER WORDS, THERE'S A SMALL NUMBER OF PEOPLE,

22 THERE'S A SMALL NUMBER OF PEOPLE IN TABLE ONE IN

23 THAT PAPER THAT HAVE A NORMAL SEROTONIN IN THE

24 URINE OR LESS THAN TWICE NORMAL -- NORMAL OR LESS

25 THAN TWICE NORMAL 5-HIAA IN THE URINE THAT HAVE

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1 MORE STRIKING ELEVATIONS OF THE SEROTONIN IN THE
2 URINE.
3 Q. THEY FALL WITHIN THAT ATYPICAL CARCINOID
4 GROUP?
5 A. THEY WOULD FALL INTO THE, YES, BIOCHEMICAL
6 SENSE ATYPICAL CARCINOID GROUP.
7 Q. IS THERE ANY OTHER REASON THAT YOU CAN
8 ASCRIBE TO TUMORS THAT WOULD HAVE AN INCREASE IN
9 URINE AND A NORMAL BLOOD 5-HT LEVEL?
10 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
11 THE WITNESS: THERE'S AN OCCASIONAL
12 PATIENT WHERE IT'S JUST THAT THE URINE IS HIGHER
13 THAN THE BLOOD FOR NO EXPLANATION. THERE'S A RARE
14 PATIENT WHERE THIS OCCURS WHERE IT DOESN'T SEEM TO
15 BE ATYPICAL OR A MATTER OF A MEDICATION BUT IT
16 JUST HAPPENS THAT THE BLOOD LEVEL WILL BE A LITTLE
17 HIGHER. BUT, IN GENERAL, THE URINE IS, YOU KNOW,
18 MORE SENSITIVE. SO THERE'S THE CATEGORY I TALKED
19 ABOUT, DRUGS, ATYPICAL, AN OCCASIONAL PATIENT THAT
20 FOR SOME REASON THE BLOOD IS HIGHER, AND THAT
21 WOULD BE THE ONLY THREE CATEGORIES I CAN THINK
22 OF.
23 BY MS. WALTERS:
24 Q. ARE THERE PATIENTS THAT HAVE ELEVATED 5-HTP
25 BUT HAVE NORMAL 5-HT AND NORMAL 5-HIAA READINGS,

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1 AGAIN, LUNG CANCER PATIENTS OR LUNG TUMOR
2 PATIENTS?
3 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
4 THE WITNESS: I DON'T KNOW THAT I CAN
5 ANSWER THAT WITH LUNG TUMOR PATIENTS. I'VE LOOKED
6 AT IT MORE WITH CARCINOID PATIENTS, CARCINOID
7 TUMOR PATIENTS.
8 BY MS. WALTERS:
9 Q. HOW ABOUT CARCINOID TUMORS OF THE LUNG?
10 A. CARCINOID TUMORS OF THE LUNG? LET'S SEE.
11 IN MY EXPERIENCE AND AS CITED IN THIS PAPER,
12 CLINICAL CHEMISTRY PAPER, ALL THE PATIENTS WITH
13 INCREASED URINARY EXCRETION OF 5-HTP HAD INCREASED
14 SECRETION OF SEROTONIN. FOUR OF THE PATIENTS WITH
15 INCREASED URINARY EXCRETION OF SEROTONIN HAD
16 NORMAL LEVELS FOR 5-HTP. SO IN GENERAL -- I'VE
17 FORGOTTEN BECAUSE OF A LONG-WINDED ANSWER. IN
18 GENERAL, WHAT WAS THE QUESTION WE STARTED WITH?
19 I'M SORRY.
20 MS. WALTERS: READ THE QUESTION
21 BACK.
22 (DESIGNATED QUESTION IS READ)
23 BY MS. WALTERS:
24 Q. ELEVATED 5-HTP, NORMAL 5-HT AND NORMAL
25 5-HIAA READINGS.

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1 A. WELL, MY EXPERIENCE IS THAT ALL THE PATIENTS
2 WHO HAD ELEVATED 5-HTP ALSO HAD ELEVATED 5-HT
3 LEVELS, BUT NOT ALL THE PATIENTS WHO HAD ELEVATED
4 5-HT LEVELS HAD ELEVATED ELEVATED 5-HTP LEVELS.
5 AND I THINK THESE TWO MEASUREMENTS ARE FAIRLY
6 EQUIVALENT IN THE INFORMATION THAT THEY GIVE ONE.
7 BUT IN MY LAB, THE 5-HT IS TECHNICALLY EASIER TO
8 MEASURE. AND THEY GIVE YOU IN GENERAL SIMILAR
9 INFORMATION WITH THE 5-HT AS BEING MORE
10 SENSITIVE. SO I TEND TO -- MY CURRENT PRACTICE IS
11 TO DO THE 5-HT AND NOT THE 5-HTP BECAUSE EVERYONE
12 WHO'S BEEN HIGH ON 5-HTP WAS ALSO HIGH ON 5-HT.
13 Q. HOW MANY ARE YOU TALKING ABOUT, CARCINOIDS
14 OF THE LUNG?
15 A. I'M TALKING ABOUT 26 PATIENTS WHERE WE
16 MEASURED 5-HT, 5-HTP AND 5-HIAA, BUT I DON'T KNOW
17 HOW MANY OF THOSE -- THAT WAS THE THING THAT WAS
18 REMOVED FROM THIS PAPER AND I DON'T KNOW HOW MANY
19 OF THOSE WERE CARCINOMA OF THE LUNG -- CARCINOID
20 OF THE LUNG.
21 Q. WELL, WE KNOW YOU HAD A TOTAL OF EIGHT LUNG
22 CARCINOIDS?
23 A. RIGHT. BUT I DON'T KNOW HOW MANY OF THOSE
24 26 INCLUDE -- HOW MANY OF THE EIGHT ARE INCLUDED
25 IN THE 26. IS THAT SOMETHING YOU WERE REQUESTED

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1 TO SEE IF WE CAN GET?

2 MR. SIRRIDGE: I CAN'T RECALL.

3 MS. WALTERS: YES, IT WAS.

4 THE WITNESS: SO I COULD ANSWER IT

5 ONLY IN TERMS OF THE OVERALL CARCINOIDS, YOU

6 KNOW. OVERALL CARCINOID PATIENTS THAT THE 5-HT

7 WAS. BUT I CAN'T BREAK IT DOWN AT THE MOMENT INTO

8 THE BRONCHIAL CARCINOIDS WITHOUT LOOKING AND

9 TRYING TO FIND THAT INFORMATION ON EITHER THAT

10 TABLE OR FIGURE.

11 BY MS. WALTERS:

12 Q. WOULD YOU EVER EXAMINE THAT RELATIONSHIP IN

13 ANY OTHER PAPERS OR STUDIES?

14 A. I ALSO THINK I EXAMINED IT IN THE PAPER IN

15 GASTROENTEROLOGY THAT WE TALKED ABOUT EARLIER. MY

16 RECOLLECTION IS THAT'S AN OLDER PAPER BUT I

17 EXAMINED IT -- I DON'T SEE IT DESCRIBED IN THE

18 TEXT IN THAT PAPER. IT LOOKS LIKE IN THAT PAPER,

19 I ONLY DID IT IN THE ONES THAT WERE THE CLASSICAL

20 ATYPICAL. I MEASURED THE -- HERE IT IS. I

21 ACTUALLY DID IT ON ALL THE PATIENTS. SO IT'S ON

22 PAGE 1111, TABLE ONE AND TABLE TWO. AGAIN, IT

23 LOOKS TO ME LIKE THE 5-HT IS MORE SENSITIVE --

24 Q. TAKE A LOOK AT PATIENT NUMBER THREE.

25 A. RIGHT.

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1 Q. PATIENT NUMBER THREE HAS A NORMAL 5-HT
2 LEVEL; ISN'T THAT CORRECT?
3 A. YES, THAT'S CORRECT.
4 Q. AND IT HAS AN ELEVATED 5-HTP?
5 A. YES, YES. AT THAT TIME I WAS USING A
6 DIFFERENT METHOD. IT WAS A FLUOROMETRIC METHOD
7 FOR 5-HT. AND I ACTUALLY HAD A NORMAL HIGHER
8 RANGING UP TO TWO HUNDRED 50 MICROGRAMS, 40 TO TWO
9 HUNDRED 50. AND, CURRENTLY, THE METHOD I USE IS A
10 RADIOENZYMATIC METHOD THAT'S MORE PRECISE AND
11 SENSITIVE AND I BELIEVE I CAN NOW DO A BETTER JOB
12 THAN I DID THEN IN MEASURING THE 5-HT.
13 Q. AND SOME OF THE NON-BRONCHIAL CARCINOIDS
14 HAVE A NORMAL 5-HT BUT A HIGH OR AN ELEVATED
15 5-HTP; IS THAT CORRECT? LOOK AT NUMBER TWO, FOR
16 EXAMPLE.
17 A. YES, THAT SEEMS TO BE CORRECT. THAT SEEMS
18 TO BE CORRECT IN THE WAY THAT WAS MEASURED, WITH A
19 DIFFERENT METHODOLOGY THEN, SOMEWHAT DIFFERENT
20 METHODOLOGY.
21 Q. SO THERE ARE PATIENTS WITH CARCINOIDS OF THE
22 LUNG THAT CAN HAVE AN ELEVATED 5-HTP BUT A NORMAL
23 5-HT LEVEL?
24 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
25 THE WITNESS: ACTUALLY, IN THAT

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1 STUDY, ALL THE PATIENTS THAT HAD CARCINOIDS OF THE
2 LUNG SEEM TO BE ELEVATED -- THERE'S ONLY FOUR ON
3 THAT TABLE.
4 BY MS. WALTERS:
5 Q. AND ONE OF THE FOUR HAD A NORMAL 5-HT AND AN
6 ELEVATED 5-HTP, CORRECT, PATIENT NUMBER THREE?
7 A. ONE OF THE FOUR WITH THAT METHOD HAD A
8 NORMAL 5-HT AND AN ELEVATED 5-HTP IN THE URINE,
9 THAT'S CORRECT. THE OTHER THREE, THE OTHER THREE
10 OF THE FOUR WERE ELEVATED ON BOTH THINGS. THAT'S
11 CORRECT.
12 Q. DO YOU EVER SEE -- CAN PATIENTS HAVE AN
13 ELEVATED 5-HTP AND AN ELEVATED 5-HT AND A NORMAL
14 URINE 5-HIAA?
15 MR. SIRRIDGE: I THINK THAT'S BEEN
16 ASKED AND ANSWERED.
17 MS. WALTERS: IT'S A DIFFERENT
18 QUESTION.
19 MR. SIRRIDGE: WHAT BODILY FLUID ARE
20 WE TALKING ABOUT?
21 BY MS. WALTERS:
22 Q. URINE.
23 A. URINE. I THINK I ALREADY ANSWERED THAT AND
24 SAID IT CAN HAPPEN ON OCCASION. IT'S DEMONSTRATED
25 IN TABLE ONE ON PAGE 842 OF THE CLINICAL CHEMISTRY

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1 PAPER WHERE THERE WERE SOME PEOPLE THAT FULFILLED
2 THOSE CRITERIA.
3 Q. HAS ANYBODY EVER STUDIED THE DIFFERENT
4 COMBINATIONS OF ELEVATION OF THESE CHEMICALS AS
5 FAR AS YOU KNOW?
6 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
7 THE WITNESS: STUDIED THEM IN WHAT
8 WAY, IN OTHER WORDS AS FAR AS THEIR DIAGNOSTIC
9 UTILITY OR --
10 BY MS. WALTERS:
11 Q. NO. THE NUMBERS OF, FOR EXAMPLE, OF LUNG --
12 CARCINOIDS OF THE LUNG THAT HAVE ELEVATED LEVELS
13 OF CERTAIN CHEMICALS AND NOT ELEVATED LEVELS OF
14 OTHER CHEMICALS AND DRAWN ANY CONCLUSIONS ABOUT
15 PATTERNS?
16 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
17 THE WITNESS: I THINK I'VE PROBABLY
18 BEEN ONE OF THE MAIN PEOPLE THAT HAVE STUDIED THAT
19 OVER THE YEARS. I DON'T KNOW OF ANYONE ELSE THAT
20 HAS STUDIED THAT WITHIN THE SAME WAY.
21 BY MS. WALTERS:
22 Q. AND YOU'VE INDICATED, I THINK, THAT YOU HAVE
23 NOTED A PATTERN OF PRESENTATION THAT YOU'VE
24 LABELED, AND I THINK IT'S BEEN LABELED ELSEWHERE
25 IN THE LITERATURE, AS AN ATYPICAL CARCINOID?

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1 A. BIOCHEMICALLY ATYPICAL CARCINOID, YES.
2 Q. SO THE CHEMICALS THAT WE'RE DISCUSSING, THE
3 SEROTONIN AND THEIR METABOLITES, CAN APPEAR IN
4 DIFFERENT COMBINATIONS IN DIFFERENT TUMORS?
5 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
6 BY MS. WALTERS:
7 Q. ISN'T THAT CORRECT?
8 A. WELL, YOU'RE ASKING A QUESTION ABOUT THE
9 TUMORS AND RATHER THAN -- I DON'T KNOW IF I CAN
10 ANSWER IT BETTER WITH RESPECT TO THE BLOOD AND THE
11 URINE.
12 Q. I DON'T KNOW WHAT YOU MEAN.
13 A. WELL, I GUESS I DON'T UNDERSTAND HOW YOU
14 WANT ME TO ANSWER -- WHAT ANSWER YOU'RE LOOKING
15 FOR WITH YOUR QUESTION BECAUSE YOU SAID IN THE
16 TUMORS.
17 Q. 5-HTP MAY OR MAY NOT BE ELEVATED IN A GIVEN
18 CARCINOID OF THE LUNG?
19 A. THAT'S CORRECT.
20 Q. AND IT MAY OR MAY NOT BE ELEVATED IN A SMALL
21 CELL CANCER, ALTHOUGH THERE'S MUCH LESS DATA ON
22 THAT?
23 A. THAT'S CORRECT.
24 Q. AND 5-HT MAY OR MAY NOT BE ELEVATED IN A
25 GIVEN CARCINOID TUMOR OF THE LUNG?

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1 A. THAT'S RIGHT. THE ONLY THING I WOULD LIKE
2 TO SAY IS THERE'S VERY FEW MEASUREMENTS OF 5-HTP
3 IN CARCINOID TUMORS OF THE LUNG THAT ARE IN THE
4 LITERATURE THAT I'M AWARE OF. THERE ARE
5 MEASUREMENTS OF 5-HT BUT NOT VERY MANY OF 5-HTP.
6 Q. AND 5-HT MAY OR MAY NOT BE ELEVATED IN A
7 GIVEN SMALL CELL CANCER OF THE LUNG BUT, AGAIN,
8 THERE IS A LOT LESS DATA ON THAT; ISN'T THAT
9 CORRECT?
10 (OBJECTION) MR. SIRRIDGE: I'M GOING TO OBJECT TO
11 THE FORM. I DON'T KNOW WHAT YOU MEAN BY "A LOT
12 LESS DATA".
13 BY MS. WALTERS:
14 Q. A LOT LESS PUBLISHED DATA ON THE LEVELS OF
15 5-HT IN SMALL CELL CANCERS THAN THERE IS IN
16 CARCINOIDS; ISN'T THAT CORRECT?
17 A. OFF THE TOP OF MY HEAD, I DON'T KNOW OF ANY
18 STUDIES THAT HAVE SHOWN THE SEROTONIN TO BE
19 ELEVATED IN SMALL CELL CANCERS USING QUANTITATIVE
20 METHODS OF MEASUREMENT. NOW SOME OF THEM MIGHT
21 HAVE DONE IT WITH THE HISTOCHEMICAL FLUORESCENCE,
22 AND SOME STUDIES WE REFERRED TO EARLIER, THE ONES
23 THAT CAME UP FOUR YEARS AFTER CARCINOIDS AND
24 SEROTONIN WERE ASSOCIATED, THEY TALKED ABOUT SMALL
25 CELL CARCINOMAS WITH SEROTONIN OR 5-HIAA IN THE

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1 URINE, THAT TYPE THING. BUT I'M NOT AWARE OF ANY
2 THAT MEASURED IT QUANTITATIVELY IN THE TUMORS.
3 I'M NOT AWARE OF IT FROM MY KNOWLEDGE OF THE
4 LITERATURE QUANTITATIVELY. THAT'S WHY IT'S HARD
5 FOR ME TO ANSWER THAT.
6 Q. BUT 5-HT MAY OR MAY NOT BE ELEVATED IN A
7 GIVEN SMALL CELL CANCER?
8 MR. SIRRIDGE: BASED ON WHAT?
9 BY MS. WALTERS:
10 Q. BASED ON ANYTHING.
11 MR. SIRRIDGE: LITERATURE OR DR.
12 FELDMAN'S WORD? WHAT I'M CONFUSED ABOUT -- GO
13 AHEAD.
14 THE WITNESS: SEE, MY THING, I WOULD
15 SAY -- WHEN YOU SAY "MAY OR MAY NOT", I AM NOT
16 AWARE OF ANY THAT IT IS ELEVATED SO I WOULD SAY IT
17 MAY NOT BECAUSE I DON'T KNOW OF ANY REPORTS FROM
18 THE LITERATURE AND I HAVE NEVER, TO MY
19 RECOLLECTION, FOUND IT ELEVATED, ALTHOUGH I WAS
20 GOING TO LOOK WHEN I GOT HOME, BUT I HAVE NOT
21 RECALLED. AS FAR AS I KNOW, MINE WERE ALWAYS
22 NORMAL AND I CAN'T RECALL THE LITERATURE BEING
23 ELEVATED IN THE TUMOR.
24 BY MS. WALTERS:
25 Q. HOW ABOUT IN THE URINE OR THE BLOOD? I

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1 WASN'T REALLY LIMITING IT TO THE TUMOR.

2 A. OKAY. THE URINE OR THE BLOOD, EARLIER IN

3 THE DEPOSITION WHEN WE TALKED ABOUT WHEN YOU ASKED

4 ME IF THERE WAS AS ASSOCIATION, WHEN WERE

5 CARCINOIDS ASSOCIATED WITH SEROTONIN AND THEN WHEN

6 WERE BRONCHIALS AND THEN WHEN WERE SMALL CELLS,

7 AND I THINK THEY WERE ASSOCIATED IN THE URINE

8 AROUND APPROXIMATELY FOUR YEARS AFTER THEY WERE

9 ASSOCIATED WITH CARCINOIDS IN GENERAL. AND I

10 THINK THAT WAS IN SOME REPORTS EMANATING FROM

11 ENGLAND, IN THE LANCET OR SOME OTHER JOURNAL LIKE

12 THAT. I CAN RECALL REPORTS OF THAT NATURE BUT I

13 CAN'T RECALL THAT THEY ACTUALLY MEASURED IT IN THE

14 SMALL CELL TUMOR. I DON'T HAVE ANY RECOLLECTION

15 OF PEOPLE MEASURING IT IN THE SMALL CELL JUST

16 MEASURING IT IN THE URINE.

17 Q. AND THE 5-HIAA LEVEL MAY OR MAY NOT BE

18 INCREASED IN A CARCINOID TUMOR OF THE LUNG?

19 A. YES, I PERSONALLY HAVE NOT MEASURED THE

20 5-HIAA IN THE CARCINOID TUMORS. I'VE ONLY

21 MEASURED THE SEROTONIN AND THE

22 5-HYDROXYTRYPTOPHAN.

23 Q. MY QUESTION WAS CONFUSING. I MEANT 5-HIAA

24 IN THE URINE HAVE NOT BEEN ELEVATED OR -- LET ME

25 START OVER.

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1 THE 5-HIAA URINE LEVEL MAY OR MAY NOT BE
2 ELEVATED IN A CARCINOID TUMOR OF THE LUNG?
3 A. THAT IS CORRECT. THAT'S CORRECT.
4 Q. AND THE URINE 5-HIAA LEVEL MAY OR MAY NOT BE
5 ELEVATED IN A SMALL CELL CANCER OF THE LUNG?
6 A. THAT WOULD BE CORRECT, YES, I WOULD SAY SO.
7 Q. IS THERE ANY -- BASED ON YOUR EXPERIENCE OR
8 YOUR UNDERSTANDING OF THE LITERATURE, WHEN WOULD
9 ANY OF THESE LEVELS BE ELEVATED IN ANY OF THESE
10 TUMORS CLINICALLY, IS THERE ANY CLINICAL
11 CORRELATION?
12 (OBJECTION) MR. SIRRIDGE: I'M GOING TO OBJECT TO
13 THE FORM. I DON'T HAVE ANY IDEA WHAT "THESE
14 LEVELS" AND "THESE TUMORS" MEAN AFTER THAT LONG
15 LIST OF QUESTIONS.
16 BY MS. WALTERS:
17 Q. I'M TALKING ABOUT 5-HT, 5-HTP AND 5-HIAA IN
18 THE URINE, IN THE BLOOD, IN THE TUMOR ITSELF. IS
19 THERE ANY WAY THAT ANYBODY CAN SAY WHEN THESE
20 SUBSTANCES WOULD BE ELEVATED IN A GIVEN TUMOR FROM
21 A CLINICAL STANDPOINT?
22 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
23 YOU MAY ANSWER IT, IF YOU CAN UNDERSTAND IT.
24 THE WITNESS: OKAY. THEY MIGHT BE
25 ELEVATED. THESE SUBSTANCES MIGHT BE ELEVATED, ONE

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1 MIGHT SUSPECT THEY MIGHT BE ELEVATED IF THE
2 PATIENT HAD SYMPTOMS OF THE CARCINOID SYNDROME,
3 SUCH AS THE COMMON ONES IN MY EXPERIENCE ARE
4 DIARRHEA AND FLUSHING. IF ONE HAD THOSE THINGS,
5 THEN ONE MIGHT SAY THAT THOSE CARCINOID TUMORS ARE
6 MORE LIKELY TO HAVE ELEVATED SEROTONIN IN THE
7 TUMOR AND PARTICULARLY 5-HIAA IN THE URINE AND SO
8 FORTH IN THE BLOOD. IF THERE WAS A CLINICAL
9 CORRELATE, THEN IT WOULD BE MORE LIKELY. IF THERE
10 WASN'T CLINICAL SYMPTOMS, IT STILL IS POSSIBLE
11 IT'S ELEVATED, BUT IT WOULD BE, YOU KNOW, IT WOULD
12 BE LESS STATISTICALLY LIKELY. I DON'T KNOW IF
13 THAT ANSWERS YOUR QUESTION.
14 BY MS. WALTERS:
15 Q. IT'S MORE LIKELY TO FIND AN ELEVATION IN
16 THESE -- OF THESE CHEMICALS IN A PATIENT THAT HAS
17 THE CARCINOID SYNDROME; IS THAT CORRECT?
18 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
19 HE SAID SYMPTOMS OF THE CARCINOID SYNDROME.
20 THE WITNESS: IS IT MORE LIKELY TO
21 FIND THESE CHEMICALS ELEVATED? YES, IT WOULD BE
22 MORE LIKELY TO FIND THEM ELEVATED IN PATIENTS THAT
23 HAD THE SYMPTOMS OF THE CARCINOID SYNDROME.
24 BY MS. WALTERS:
25 Q. WHAT PERCENTAGE OF LUNG CANCER PATIENTS HAVE

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1 THE CARCINOID SYNDROME -- STRIKE THAT.

2 WHAT PERCENTAGE OF LUNG CARCINOID PATIENTS

3 HAVE CARCINOID SYNDROME?

4 MR. SIRRIDGE: YOU'RE LIMITING IT TO

5 THE SYNDROME?

6 MS. WALTERS: YES.

7 THE WITNESS: THE SYNDROME MAY BE

8 CONSIDERED TO HAVE FLUSHING AND DIARRHEA. OR I

9 ALSO CONSIDER IT A PARTIAL SYNDROME IF THEY HAVE

10 EITHER FLUSHING OR DIARRHEA. AT THE MOMENT, I

11 DON'T HAVE WITH ME THE PRECISE FIGURES ABOUT WHAT

12 PERCENTAGE OF THE BRONCHIAL CARCINOIDS WOULD HAVE

13 THE SYNDROME. OVERALL, AND I DON'T HAVE THIS DATA

14 WITH ME, OVERALL, I WOULD SAY THAT APPROXIMATELY

15 50 PERCENT OF THE OVERALL PATIENTS WITH CARCINOID

16 TUMORS THAT HAVE --

17 BY MS. WALTERS:

18 Q. WOULD HAVE THE SYNDROME OR SYMPTOMS OF THE

19 SYNDROME?

20 A. WELL, LET ME START THAT OVER. PATIENTS WITH

21 CARCINOID TUMORS, BRONCHIAL CARCINOID TUMORS --

22 SEE, I WOULD HAVE TO BE TAKING AN ESTIMATE ON IT.

23 IF I HAD THE DATA I HAD AT HOME, I COULD GIVE A

24 PRECISE SORT OF A THING.

25 Q. YOU DON'T KNOW; IS THAT YOUR ANSWER?

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1 A. I DON'T KNOW. I DON'T KNOW. I WOULD SAY --
2 Q. DO YOU KNOW WHAT PERCENTAGE OF PATIENTS
3 WITH --
4 A. THE PATIENTS THAT HAD -- THAT DID NOT HAVE
5 THE ELEVATED SEROTONIN OR 5-HIAA THAT I LISTED IN
6 THAT BENIGN BRONCHIAL CARCINOID, I WOULD SAY
7 VIRTUALLY NONE OF THOSE PATIENTS WOULD HAVE
8 DIARRHEA OR FLUSHING, THOSE 32 PATIENTS, THOSE 32
9 I CAN RECALL THAT. NOW, IF WE LOOK AT THESE
10 PATIENTS THAT HAVE ELEVATED LEVELS -- I HAVE IT
11 ACTUALLY ON ONE OF THE SHEETS IN THE EXHIBIT. I
12 DIDN'T PUT IT ON THE ONES WITH THE BENIGN COURSE
13 BECAUSE VIRTUALLY NONE OF THEM HAD IT. BUT OF
14 THESE PATIENTS, LET'S SEE AND GO DOWN THE LIST
15 HERE. THERE'S ONE WITH DIARRHEA. ONE WITH BOTH.
16 NINE OF -- NINE OF THE 19 PATIENTS IN THAT LIST
17 HAD EITHER DIARRHEA OR FLUSHING OR BOTH.
18 Q. WAS IT NINE OF 19 PATIENTS WITH METASTATIC
19 DISEASE?
20 A. NINE OF 19 PATIENTS THAT HAD METASTATIC
21 DISEASE, THAT'S CORRECT.
22 Q. DID THEY HAVE METASTATIC DISEASE AT THE TIME
23 THEY HAD THE SYMPTOMS?
24 A. NOT NECESSARILY.
25 Q. AND NONE OF THE PATIENTS THAT DID NOT HAVE

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1 METASTATIC DISEASE HAD THE SYMPTOMS; IS THAT
2 CORRECT?
3 A. OH, HERE IT IS. ONE PATIENT. THIS WAS THE
4 FIRST PAGE. ONE PATIENT I HAVE LISTED AS HAVING
5 FLUSHING THAT DID NOT HAVE -- THAT HAD A BENIGN
6 COURSE, ONE PATIENT OUT OF THE 32, AND THAT
7 PATIENT DID NOT HAVE ELEVATED 5-HIAA. SHE DID NOT
8 -- SHE HAD FLUSHING. ONLY ONE.
9 Q. BASED ON THOSE NUMBERS, DO YOU HAVE A
10 STATISTIC AS TO THE NUMBER OF BRONCHIAL CARCINOIDS
11 THAT HAVE THE CARCINOID SYNDROME?
12 A. OKAY. YES. WHAT DID WE END UP WITH HERE,
13 NINE? HOW MANY DID I SAY -- I GUESS I CAN SAY HOW
14 MANY --
15 MR. SIRRIDGE: YOU SAID NINE.
16 BY MS. WALTERS:
17 Q. NINE OF 19.
18 A. SO WE'VE GOT NINE OF 19 AND ONE MORE IS
19 TEN. AND IT'S TEN OF 32. 51. SO IT'S TEN OF 51
20 WOULD HAVE SOME MANIFESTATION OF THE CARCINOID
21 SYNDROME. THAT'S 20 PERCENT.
22 Q. YOU THINK THAT'S WHAT THE LITERATURE
23 REFLECTS?
24 A. I THINK THAT THE LITERATURE IS SO DIVERSE
25 THAT DEPENDING ON HOW THE DATA IS COLLECTED, IT

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1 MAY NOT REFLECT THAT. IN OTHER WORDS, IF IT WAS
2 COLLECTED BY A THORACIC SURGEON WHO DIDN'T HAVE A
3 LOT OF PEOPLE WHO HAD MORE EXTENSIVE DISEASE, HE
4 WOULDN'T FIND 20 PERCENT BECAUSE ALMOST ALL THE
5 ONES THAT HAD THE SYNDROME HAD THE EXTENSIVE
6 DISEASE. I DON'T KNOW THAT THEY HAD THE
7 METASTATIC DISEASE WHEN THEY FIRST GOT THE
8 FLUSHING AND DIARRHEA BUT IT WOULD BE IN THAT
9 GROUP THAT HAD MORE DISEASE.
10 Q. WOULD IT ALSO BE TRUE THAT THE PATIENTS MOST
11 LIKELY TO HAVE ELEVATED LEVELS OF THE CHEMICALS
12 THAT WE'RE TALKING ABOUT, INCLUDING 5-HTP, 5-HT
13 AND 5-HIAA, WOULD BE PATIENTS WITH METASTATIC
14 DISEASE?
15 A. THEY WOULD BE MORE LIKELY TO, BUT THEY
16 WOULDN'T BE RESTRICTED TO THAT. I CAN NOW RECALL
17 ONE PATIENT ON THIS LIST WHO AT THE TIME HE HAD A
18 CLINICALLY-LIMITED TUMOR HAD FLUSHING AND
19 DIARRHEA. HE WOULD HAVE BEEN THIS PATIENT WHO
20 LIVED FOR A HUNDRED AND 34 MONTHS AND HAD A 5-HIAA
21 VALUE OF 475. HE ACTUALLY HAD FLUSHING AND
22 DIARRHEA WHEN HIS TUMOR WAS FIRST DISCOVERED. AND
23 AT THAT TIME, THERE WASN'T ANY CLINICAL EVIDENCE
24 THAT HE HAD METASTATIC DISEASE.
25 Q. WERE THE MEASUREMENTS OF HIS SEROTONIN AND

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1 5-HIAA ALSO TAKEN AT A TIME WHEN HE HAD LIMITED
2 DISEASE?
3 A. THEY WERE NOT TAKEN BY ME AT THAT TIME.
4 THAT WAS BEFORE I FIRST ENCOUNTERED THE PATIENT.
5 Q. SO THOSE MEASUREMENTS WERE TAKEN WHEN HE
6 ALREADY HAD METASTATIC DISEASE?
7 A. YES. THESE MEASUREMENTS WERE TAKEN WHEN HE
8 HAD METASTATIC DISEASE, THESE MEASUREMENTS THAT
9 ARE LISTED HERE.
10 Q. IS THAT TRUE WITH ALL THESE PATIENTS?
11 MR. SIRRIDGE: HE'S ALREADY TESTIFIED
12 THAT SOME OF THEM AREN'T METASTATIC PATIENTS SO IT
13 COULDN'T POSSIBLY BE.
14 THE WITNESS: ALL OF THESE ARE
15 METASTATIC PATIENTS AT THE TIME, BUT THE NUMBER
16 MAY NOT BE TAKEN. IN GENERAL, THE NUMBER IS THE
17 FIRST VALUE I GET ON THE PATIENT. IF IT TURNS OUT
18 THAT THE PATIENT LATER, BECAUSE HE HAS SUCH A
19 SMALL TUMOR, HAS A NORMAL VALUE AND LATER DEVELOPS
20 AN ELEVATED VALUE, I'M REALLY INTERESTED IN HOW
21 MANY TUMORS CAN POTENTIALLY PRODUCE SEROTONIN. IF
22 THAT HAPPENS, I'LL UPDATE THE TUMOR TO PUT IN A
23 HIGHER VALUE.
24 BY MS. WALTERS:
25 Q. SO SOME OF THE TUMORS, THIS MALIGNANT

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1 BRONCHIAL TUMOR LIST OF 19 ORIGINALLY HAD NORMAL
2 READINGS AND LATER HAD ABNORMAL READINGS; IS THAT
3 CORRECT?
4 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
5 THE WITNESS: I CANNOT SPEAK
6 SPECIFICALLY ABOUT THIS LIST. I CANNOT SPEAK
7 SPECIFICALLY ABOUT THIS LIST. I KNOW THAT IN
8 OTHER PATIENTS, I HAVE PATIENTS WITH ALL SORTS OF
9 CARCINOID TUMORS, AND WHAT I WILL DO, MY PRACTICE
10 IS I'LL PUT IN THE FIRST VALUE I GET ON THEM AND
11 I'LL LEAVE THAT IN.
12 BUT IF AT A LATER DATE THEY HAVE A
13 HIGH VALUE, I WILL SUBSTITUTE ALL THE VALUES THAT
14 CAME WHEN THAT HIGH VALUE OCCURRED BECAUSE I WANT
15 TO KNOW THE MAXIMUM NUMBER OF PATIENTS THAT COULD
16 BE PRODUCING SEROTONIN, AND IT COULD BE THAT THEY
17 WERE NORMAL AT THAT TIME BECAUSE THEY HAD TOO
18 LITTLE TUMOR TO BE ELEVATED. NOW, I CAN'T SAY
19 SPECIFICALLY ON THAT LIST. I CAN ONLY TELL YOU
20 THAT'S MY GENERAL -- THE GENERAL WAY I DO IT.
21 BY MS. WALTERS:
22 Q. SO ALL OF THESE LISTS -- THE NUMBERS ON THIS
23 LIST WOULD AT LEAST BE THE MAXIMUM VALUE OBTAINED
24 FOR ANY ONE PATIENT?
25 A. NO. IT WOULDN'T BE THE MAXIMUM VALUE

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1 BECAUSE ONCE THEY GOT A VALUE THAT WAS ABOVE
2 NORMAL, EVEN THOUGH THEY GO HIGHER, I DON'T
3 INCREASE THEM ANYMORE. IN OTHER WORDS, IF THE
4 5-HIAA GOT TO BE 10 OR GOT TO BE 15, THE PATIENT
5 COULD LATER GET ONE THAT COULD BE TWO HUNDRED AND
6 50. I MIGHT HAVE THAT RECORD IN A LONGITUDINAL
7 RECORD NOT IN MY COMPUTER BUT I WOULDN'T CHANGE
8 THAT NUMBER. BUT IF THEY STARTED OUT AT TWO, AND
9 LATER AS THE TUMOR GREW IT GOT UP TO 15, I WOULD
10 ENTER THE 15.
11 Q. WHAT IF THE ORIGINAL READING WAS A TWO, THE
12 SECOND READING WAS A 15 WHICH YOU ENTERED ON THIS
13 CHART AND A SUBSEQUENT READING WAS A TWO, WOULD
14 YOU THEN RETURN IT, CHANGE IT TO A TWO?
15 A. THAT'S ACTUALLY NEVER HAPPENED TO ME.
16 Q. WHY IS THAT?
17 A. WELL, BECAUSE WHAT HAPPENS IS THE TUMOR
18 GROWS. AND ONCE IT GETS ABOVE THE VALUE -- OKAY.
19 IF I HAVE GIVEN THESE PATIENTS -- IF THEY HAVE
20 RECEIVED CHEMOTHERAPY AND THEY FALL, AND THEY GOT
21 UP TO A 15 AND THEY FELL TO AN 8, I WOULDN'T
22 CHANGE THE NUMBER. I WOULD NOT CHANGE THE
23 NUMBER. THAT HAS HAPPENED ON OCCASION WITH
24 EFFECTIVE CHEMOTHERAPY. BUT MY MAIN INTEREST IN
25 KEEPING THIS PARTICULAR DATA IS TO FIND OUT WHAT'S

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1 THE MAXIMUM NUMBER OF PATIENTS THAT HAVE TUMORS
2 THAT ARE CAPABLE OF PRODUCING SEROTONIN. SO I
3 WOULDN'T CHANGE THAT IN THE RECORD. I MIGHT HAVE
4 A -- I USUALLY HAVE A LONGITUDINAL RECORD, A FLOW
5 SHEET ON THESE PATIENTS SHOWING THAT THEY DROPPED
6 FROM 15 DOWN TO TWO, AND THEN I MIGHT FOLLOW THEM
7 FOR FOUR, FIVE, TEN YEARS. BUT MY PRACTICE IS --
8 Q. CHEMOTHERAPY MIGHT REDUCE THE NUMBER THEN;
9 IS THAT CORRECT?
10 A. IT WOULD -- YOU MEAN REDUCE THE NUMBER
11 WHERE?
12 Q. THE ELEVATION OF THESE READINGS ON 5-HIAA
13 AND HT.
14 A. YES, IF IT'S SUCCESSFUL, IT WILL REDUCE THE
15 NUMBERS, BUT IT WON'T REDUCE IT IN MY DATA BASE
16 BECAUSE I DON'T -- MY PRACTICE IS NOT TO CHANGE IT
17 ONCE --
18 Q. WOULD SURGERY REDUCE THE NUMBERS?
19 A. SURGERY CAN REDUCE THE NUMBERS, YES.
20 Q. WHY IS THAT?
21 A. WELL, BECAUSE A MASS OF TISSUE IS REMOVED
22 THAT IS PRODUCING THE SEROTONIN AND THERE'S LESS
23 TISSUE PRODUCING IT AND THE VALUE WOULD THEN
24 FALL. AND I'VE HAD PATIENTS WHERE THEY'LL RESECT
25 PART OF AN UNRESECTABLE TUMOR BECAUSE THEY HAVE A

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1 BOWEL OBSTRUCTION AND THE SURGEON TAKES OUT A
2 SECTION OF THE SMALL INTESTINE AND SOME LYMPH
3 NODES, AND THAT REPRESENTS MAYBE 30 PERCENT OF
4 THEIR TUMOR. IT WAS IMPOSSIBLE FOR HIM TO REMOVE
5 ALL, BUT FOR AWHILE, THEY MAY FALL 50 PERCENT IN
6 THEIR 5-HIAA. BUT I WON'T CHANGE THAT NUMBER IN
7 MY DATA BASE.
8 Q. SO A CHEMICAL READING ON ANY PATIENT MAY
9 CHANGE, IS THAT CORRECT, EITHER UP OR DOWN
10 DEPENDING ON THE TREATMENT, DEPENDING ON THE
11 SURGERY, DEPENDING ON A NUMBER OF OTHER FACTORS?
12 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
13 THE WITNESS: IT MAY CHANGE BUT IT
14 USUALLY DOES IT IN A PREDICTABLE MANNER, THAT IS
15 WITH EXTREMELY RARE EXCEPTIONS. WHEN THE TUMOR
16 GROWS, THE CHEMICALS GO UP, AND IF YOU'RE ABLE TO
17 SUCCESSFULLY TREAT THE TUMOR, EITHER BY SURGERY OR
18 BY CHEMOTHERAPY, THE NUMBERS GO DOWN. THERE HAS
19 BEEN ONE PATIENT THAT I CAN RECALL THAT GOT MORE
20 TUMOR AND HIS TUMOR MAY HAVE BEEN -- METASTASES
21 MAY NOT HAVE BEEN ABLE TO PRODUCE THE SEROTONIN AS
22 WELL, BUT ACTUALLY HIS TUMOR MASS HAS INCREASED
23 BUT HIS 5-HIAA DIDN'T INCREASE EVEN THOSE HIS
24 TUMOR MASS INCREASED AND HE ULTIMATELY DIED FROM
25 HIS TUMOR.

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1 BY MS. WALTERS:

2 Q. DID ROSE CIPALLONE HAVE CARCINOID SYNDROME?

3 A. IN MY --

4 MR. SIRRIDGE: I DON'T THINK WE'VE

5 EVER DEFINED "CARCINOID SYNDROME".

6 MS. WALTERS: I BELIEVE HE DID DEFINE

7 IT, BUT WHETHER HE DEFINED IT OR NOT, DID ROSE

8 CIPALLONE HAVE CARCINOID SYNDROME?

9 THE WITNESS: I THINK ROSE CIPALLONE

10 HAD CARCINOID SYNDROME IN MY OPINION.

11 BY MS. WALTERS:

12 Q. WHAT IS THAT BASED ON?

13 A. THAT IS BASED ON MY KNOWLEDGE OF CARCINOID

14 SYNDROME AND MY REVIEW OF ROSE CIPALLONE'S MEDICAL

15 RECORDS.

16 Q. WHAT SPECIFICALLY -- WHAT FACTS SPECIFICALLY

17 FROM ROSE CIPALLONE'S MEDICAL RECORDS SUPPORT YOUR

18 OPINION THAT SHE HAD CARCINOID SYNDROME?

19 A. WELL, IN THE MEDICAL RECORDS, IT IS RECORDED

20 THAT ROSE CIPALLONE HAD A COMPLAINT OR A SYMPTOM

21 THAT HER DOCTOR ELICITED AS HAVING FLUSHING AND,

22 ALSO, SHE HAD A COMPLAINT OF HAVING DIARRHEA, AND

23 THOSE ARE TWO THINGS WHICH TO ME ARE THE MOST

24 PROMINENT ASPECTS OF THE CARCINOID SYNDROME.

25 Q. AND WHAT WAS THE NATURE OF THE FLUSHING THAT

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1 SHE HAD?

2 A. THE NATURE OF THE FLUSHING FROM MY CAREFUL
3 REVIEW OF THE RECORDS WAS NOT DESCRIBED IN GREAT
4 DETAIL AS I WOULD HAVE LIKED OR I WOULD HAVE
5 DESCRIBED IT. IT SAID SHE HAD FLUSHING. DR.
6 SERIFF WAS SO IMPRESSED WITH HER FLUSHING THAT HE
7 ORDERED A URINARY 5-HIAA DETERMINATION PRIOR TO
8 HER FIRST SURGERY IN AUGUST OF 1981. HE SAID SHE
9 HAD ON THE CHART FLUSHING FOR ONE YEAR. HE DID
10 NOT DESCRIBE THE NATURE OF THE FLUSHING, WHAT
11 PROVOKES THE FLUSHING, ET CETERA, NOT IN THE
12 DEGREE THAT I WOULD USUALLY DESCRIBE IT. BUT HE
13 WAS -- BUT IN HIS NOTE, HE WAS IMPRESSED ENOUGH
14 WITH HER FLUSHING THAT HE ORDERED THE 5-HIAA TEST
15 PRIOR TO THE RESECTION OF THE TUMOR. AND THE
16 HISTOLOGICAL REPORT THAT THE TUMOR WAS -- THE
17 FIRST TUMOR WAS READ AS A CARCINOID TUMOR.
18 Q. HOW OFTEN DID SHE HAVE THE FLUSHING DURING
19 THE YEAR?
20 A. AGAIN, HE DIDN'T DESCRIBE HOW FREQUENTLY SHE
21 HAD THE FLUSHING IN HIS CLINICAL NOTE. I CAN
22 REFER TO HIS NOTE, BUT MY RECOLLECTION IS THAT HE
23 NOTED IT AND THERE'S A PAUCITY OF DESCRIPTION OF
24 CERTAIN DETAILS ON SOME ASPECTS OF THE CASE.
25 Q. WHAT ABOUT THE DIARRHEA, WHAT WAS THE NATURE

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1 OF HER DIARRHEA?

2 A. WELL, CAN I GET THAT PARTICULAR SHEET? THIS

3 IS THE SHEET WHERE DR. SERIFF NOTED THAT ROSE

4 CIPALLONE HAD FLUSHING SYMPTOMS FOR ONE YEAR AND

5 DIARRHEA ON AND OFF FOR 15 YEARS AND HE DIDN'T

6 GIVE ANY FURTHER DETAILS ABOUT THAT. NOW, THE

7 THORACIC SURGEON ALSO NOTED IN HIS NOTE,

8 PARTICULARLY WITH THE SURGERY, THAT SHE HAD

9 FLUSHING SYMPTOMS, BUT, AGAIN, DID NOT GIVE

10 DETAILS ON HOW OFTEN THE FLUSHING OCCURRED OR WHAT

11 BROUGHT THE FLUSHING ON.

12 Q. IS IT YOUR TESTIMONY THAT SHE HAD CARCINOID

13 SYNDROME FOR 15 YEARS?

14 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.

15 THAT'S NOT WHAT HE TESTIFIED TO.

16 MS. WALTERS: THAT'S WHAT I WANT TO

17 KNOW. I DIDN'T ASK HIM WHAT HE TESTIFIED TO. I

18 ASKED HIM IS IT HIS OPINION.

19 THE WITNESS: THAT SHE HAD CARCINOID

20 SYNDROME FOR 15 YEARS? I DON'T KNOW HOW LONG SHE

21 HAD IT FOR. THE DIARRHEA COULD HAVE BEEN RELATED

22 TO THE TUMOR OR IT COULD HAVE BEEN NOT RELATED TO

23 THE TUMOR, ESPECIALLY SINCE IT HAD BEEN PRESENT

24 FOR 15 YEARS.

25 BY MS. WALTERS:

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1 Q. THE PRESENCE OF IT FOR 15 YEARS WOULD
2 INDICATE WHAT, THAT IT PROBABLY WAS NOT RELATED TO
3 THE TUMOR?
4 A. WELL, I HAVE HAD PATIENTS DIAGNOSED AS
5 HAVING CARCINOID TUMORS THAT HAD HISTORIES OF
6 FLUSHING GOING BACK FOR AS LONG AS 20 YEARS BEFORE
7 THE TUMOR WAS DIAGNOSED.
8 Q. WOULD THAT BE A VERY SLOW-GROWING TUMOR?
9 A. SOMETIMES THE TUMOR WILL GROW SLOWLY AT ONE
10 TIME AND THEN LATER START TO GROW MORE RAPIDLY.
11 Q. WAS THAT PATIENT A LUNG CANCER PATIENT?
12 A. I CAN RECALL SEVERAL. ONE OF THE PATIENTS
13 WHO HAD FLUSHING FOR AT LEAST TWO OR THREE YEARS
14 BEFORE HIS TUMOR WAS DIAGNOSED WAS A LUNG TUMOR
15 PATIENT. THIS OTHER PERSON WHO HAD 20 YEARS
16 BEFORE WAS A CARCINOID OF THE ILEUM BUT HE
17 ULTIMATELY DIED FROM HIS TUMOR, WHICH WAS A TUMOR
18 THAT HAD A MALIGNANT COURSE. SO I CAN'T --
19 Q. I'M ASKING ABOUT DIARRHEA. ANYBODY THAT HAD
20 DIARRHEA FOR 15 YEARS?
21 A. I CANNOT RECALL ANYONE THAT HAD DIARRHEA FOR
22 15 YEARS. I CANNOT RECALL ANYONE THAT HAD
23 DIARRHEA FOR 15 YEARS, NO.
24 Q. AND, DOCTOR, DID ROSE CIPALLONE HAVE ANY
25 NORMAL READINGS OF ANY OF THESE CHEMICALS THAT

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1 WE'VE DESCRIBED?

2 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.

3 THE WITNESS: WHAT, SPECIFICALLY,

4 CHEMICALS? WE DIDN'T DISCUSS HER CHEMICALS AT ALL

5 SO FAR, HAVE WE?

6 BY MS. WALTERS:

7 Q. NO. DID SHE HAVE ANY NORMAL READINGS?

8 A. SHE HAD -- MY REVIEW OF THE RECORD, SHE HAD

9 AT TIMES ELEVATED READINGS, AND ON OCCASIONS, SHE

10 HAD NORMAL READINGS.

11 Q. DO YOU RECALL WHEN SHE HAD THE NORMAL

12 READINGS AND WHEN SHE HAD THE ELEVATED READINGS?

13 A. YES, I DO. SHE HAD THE FIRST ELEVATED

14 READING IN AUGUST OF 1981. JUST PRIOR TO THE

15 RESECTION OF HER TUMOR, SHE HAD A READING OF 15

16 POINT FIVE WITH A NORMAL BEING ONE POINT FIVE TO

17 TEN. THAT WAS ON APPROXIMATELY THE 19TH OF

18 AUGUST, 1981.

19 Q. WOULD THAT BE CONSIDERED MINIMALLY ELEVATED?

20 A. I WOULD CONSIDER THAT MINIMALLY BUT

21 DEFINITELY ELEVATED IF DONE BY A RELIABLE

22 LABORATORY.

23 Q. WHEN WAS HER NEXT READING?

24 A. NOW, ARE WE TALKING NOW JUST ABOUT THE

25 5-HIAA OR ANYTHING?

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1 Q. ANY OF THE CHEMICALS WE'VE TALKED ABOUT.
2 A. THE NEXT READING THAT ROSE CIPALLONE HAD IN
3 MY REVIEW OF THE RECORDS WAS MAY 19, 1982, AT
4 WHICH TIME SHE HAD MEASUREMENTS MADE ON HER
5 SEROTONIN IN HER BLOOD AND TRYPTOPHAN IN HER
6 BLOOD. AND BOTH OF THOSE MEASUREMENTS WERE WITHIN
7 THE NORMAL RANGE FOR THE LABORATORY. SHOULD I
8 READ THE NORMAL RANGE?
9 Q. NO. THAT'S ALL RIGHT.
10 A. THAT WAS IN MAY 19, 1982.
11 Q. DID ROSE CIPALLONE HAVE A TUMOR IN HER BODY
12 AT THAT TIME?
13 A. SHE DID HAVE A TUMOR IN HER BODY AT THAT
14 TIME BECAUSE SHE WAS HAVING SYMPTOMS OF SOME CHEST
15 SYMPTOMS AT THE TIME. AND WITHIN A MONTH, A TUMOR
16 WAS NOTED AND SURGERY WAS PERFORMED. SO I BELIEVE
17 SHE HAD A TUMOR IN HER BODY AT THAT TIME.
18 Q. AND WAS THE TUMOR THAT WAS REMOVED A MONTH
19 LATER OR APPROXIMATELY A MONTH LATER A LARGE OR A
20 SMALL TUMOR?
21 A. FOR A PRIMARY TUMOR, THAT WOULD BE A
22 MODERATELY -- A MODERATE-SIZE TUMOR, I WOULD CALL
23 IT, USING THE TERMS IN A GENERAL SORT OF WAY. IT
24 HAD --
25 Q. IS YOUR OPINION THAT THE TUMOR THAT WAS

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1 REMOVED FROM ROSE'S LUNG IN JUNE OF 1982 A PRIMARY
2 TUMOR?
3 A. IT'S MY OPINION THAT IT'S A PRIMARY TUMOR IN
4 THAT IT WAS A RECURRENCE OF HER BRONCHIAL
5 CARCINOID TUMOR. THE ONE THAT WAS REMOVED IN
6 AUGUST OF 1981 HAD RECURRED IN JUNE OF 1982 AND
7 THAT'S WHAT WAS REMOVED.
8 Q. AND THAT WOULD STILL BE A PRIMARY TUMOR?
9 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
10 NO ONE'S EVER DEFINED "PRIMARY".
11 MS. WALTERS: WELL, THE DOCTOR USED
12 IT. I'M ASKING HIM IF THAT WOULD STILL BE A
13 PRIMARY TUMOR.
14 THE WITNESS: THAT TUMOR COULD EITHER
15 BE A LOCAL RECURRENCE OF HER ORIGINAL TUMOR OR
16 ELSE IT COULD BE A METASTASIS OF THE ORIGINAL
17 TUMOR AT THE SITE IN THE SAME LUNG WHERE THE
18 ORIGINAL TUMOR OCCURRED. NOW, I'M NOT ABLE TO
19 DISTINGUISH THOSE TWO POSSIBILITIES.
20 BY MS. WALTERS:
21 Q. NOW, WERE THOSE NORMAL READINGS THAT WERE
22 OBTAINED IN MAY OF 1982 CONSISTENT WITH A SMALL
23 CELL CANCER?
24 A. THEY COULD BE CONSISTENT WITH A LOT OF
25 THINGS.

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1 Q. ARE THEY CONSISTENT WITH SMALL CELL CANCER?
2 A. NORMAL VALUES CAN BE CONSISTENT WITH NORMAL
3 HEALTH. IT CAN BE CONSISTENT WITH SMALL CELL
4 CANCER. THEY CAN BE CONSISTENT WITH CARCINOID
5 TUMORS.
6 Q. IS IT MORE CONSISTENT WITH A SMALL CELL
7 CANCER THAN WITH A CARCINOID TUMOR?
8 A. NO.
9 Q. WHY IS THAT?
10 A. BECAUSE YOU CAN GET EXACTLY THE SAME VALUES
11 WITH A CARCINOID TUMOR.
12 Q. AND IN JUNE OF 1982 JUST BEFORE HER TUMOR
13 WAS REMOVED, SHE HAD ELEVATED URINE 5-HIAA; ISN'T
14 THAT CORRECT?
15 A. THAT IS CORRECT.
16 Q. HOW HIGH WAS THAT ELEVATION?
17 A. THAT WAS A VALUE OF 25 POINT FOUR MILLIGRAMS
18 PER 24 HOURS, THE NORMAL RANGE OF ONE POINT FIVE
19 TO TEN.
20 Q. HOW WOULD YOU CLASSIFY THAT ELEVATION?
21 A. I WOULD CLASSIFY THAT AS A MODERATE
22 ELEVATION OF 5-HIAA, MORE STRIKING THAN THE
23 ELEVATION THE YEAR BEFORE.
24 Q. AND MRS. CIPALLONE HAD AN ELEVATED URINE
25 5-HTP; IS THAT CORRECT?

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1 A. YES. THE REPORT READS THAT: SHE HAD AN
2 ELEVATED 5-HTP BY A THIN-LAYERED CHROMATOGRAM OF
3 THIS URINE DID SHOW THE PRESENCE OF A HIGH
4 CONCENTRATION OF 5-HTP BEING EXCRETED. I'M
5 QUOTING FROM THE REPORT.
6 Q. AT THE SAME TIME SHE HAD A NORMAL SEROTONIN
7 LEVEL IN THE BLOOD?
8 A. THAT IS CORRECT.
9 Q. AND A NORMAL PLASMA TRYPTOPHAN LEVEL?
10 A. THAT IS CORRECT.
11 Q. IS THAT CONSISTENT WITH WHAT YOU HAVE CALLED
12 AN ATYPICAL CARCINOID IN A BIOCHEMICAL SENSE?
13 A. YES, IT IS. IT'S COMPLETELY COMPATIBLE WITH
14 THE DIAGNOSIS OF A BIOCHEMICALLY ATYPICAL
15 CARCINOID.
16 Q. AND THIS SAME PATTERN, WOULD THAT BE
17 CONSISTENT ALSO WITH A SMALL CELL CANCER OF THE
18 LUNG?
19 A. THAT WOULD -- IT WOULD BE CONSISTENT WITH
20 THAT BUT THAT WOULD BE A MUCH RARER -- A MUCH
21 RARER EVENT TO OCCUR.
22 Q. WHY IS THAT?
23 A. WELL, BECAUSE I THINK THAT IT'S A VERY --
24 IT'S FAIRLY UNUSUAL FOR A SMALL CELL CARCINOMA TO
25 PRODUCE SEROTONIN OR 5-HYDROXYTRYPTOPHAN AND IT'S

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1 Q. ARE THEY CONSISTENT WITH SMALL CELL CANCER?

2 A. NORMAL VALUES CAN BE CONSISTENT WITH NORMAL

3 HEALTH. IT CAN BE CONSISTENT WITH SMALL CELL

4 CANCER. THEY CAN BE CONSISTENT WITH CARCINOID

5 TUMORS.

6 Q. IS IT MORE CONSISTENT WITH A SMALL CELL

7 CANCER THAN WITH A CARCINOID TUMOR?

8 A. NO.

9 Q. WHY IS THAT?

10 A. BECAUSE YOU CAN GET EXACTLY THE SAME VALUES

11 WITH A CARCINOID TUMOR.

12 Q. AND IN JUNE OF 1982 JUST BEFORE HER TUMOR

13 WAS REMOVED, SHE HAD ELEVATED URINE 5-HIAA; ISN'T

14 THAT CORRECT?

15 A. THAT IS CORRECT.

16 Q. HOW HIGH WAS THAT ELEVATION?

17 A. THAT WAS A VALUE OF 25 POINT FOUR MILLIGRAMS

18 PER 24 HOURS, THE NORMAL RANGE OF ONE POINT FIVE

19 TO TEN.

20 Q. HOW WOULD YOU CLASSIFY THAT ELEVATION?

21 A. I WOULD CLASSIFY THAT AS A MODERATE

22 ELEVATION OF 5-HIAA, MORE STRIKING THAN THE

23 ELEVATION THE YEAR BEFORE.

24 Q. AND MRS. CIPALLONE HAD AN ELEVATED URINE

25 5-HTP; IS THAT CORRECT?

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1 MUCH MORE COMMON FOR A BRONCHIAL CARCINOID, EITHER
2 TYPICAL OR ATYPICAL, TO PRODUCE THESE MATERIALS.
3 Q. IT WASN'T PRODUCING SEROTONIN, WAS IT?
4 A. IT WAS PRODUCING PREDOMINANTLY PROBABLY
5 5-HYDROXYTRYPTOPHAN. THE BLOOD SEROTONIN WAS
6 NORMAL BUT IT COULD HAVE BEEN ALSO PRODUCING SOME
7 SEROTONIN AND STILL THE BLOOD SEROTONIN COULD BE
8 NORMAL.
9 Q. BUT THE SEROTONIN READINGS ARE NORMAL HERE.
10 MR. SIRRIDGE: IN THE BLOOD.
11 THE WITNESS: IN THE BLOOD, THEY ARE
12 NORMAL. THEY WEREN'T MEASURED IN THE URINE. IT
13 SORT OF GOES BACK TO WHAT I TALKED ABOUT BEFORE
14 WHEN I SAID THERE WERE SOMETIMES GRADATIONS OF
15 CARCINOIDS BETWEEN THE CLASSICAL TYPICAL
16 BIOCHEMICALLY AND THE ATYPICAL IF ONE MEASURED
17 SOME OF THESE OTHER THINGS.
18 BY MS. WALTERS:
19 Q. COULDN'T THERE BE THE SAME VARIATIONS IN THE
20 CHEMICAL SECRETION OF A SMALL CELL CANCER?
21 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
22 THE WITNESS: THERE COULD BE, BUT,
23 YOU KNOW, AGAIN, THAT IS MUCH LESS COMMON TO HAVE
24 A SMALL CELL CARCINOMA PRODUCE THESE CHEMICALS.
25 SO IT'S CONCEIVABLE THERE COULD BE A VARIATION BUT

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1 IT JUST IS LESS LIKELY IN MY OPINION.

2 BY MS. WALTERS:

3 Q. DOCTOR, DO YOU HAVE THE MEDICAL LAB REPORT

4 FROM JUNE OF 1982?

5 A. YES, I DO.

6 Q. COULD I JUST TAKE A LOOK AT THAT?

7 A. YES (HANDING).

8 Q. DOCTOR, THE SECOND LINE OF THIS REPORT

9 STATES: THE ELEVATED 5-HIAA LEVEL DOES,

10 UNDERLINED, SUGGEST THE POSSIBILITY OF AN ATYPICAL

11 CARCINOID WHICH PRODUCES, AND THEN IT GOES ON TO

12 DESCRIBE WHAT IT PRODUCES. THE TERM "ATYPICAL

13 CARCINOID" USED IN THAT REPORT IS USED IN A

14 BIOCHEMICAL SENSE, ISN'T IT?

15 A. THAT IS CORRECT.

16 Q. IT IS NOT USED IN A HISTOLOGIC SENSE?

17 A. THAT IS CORRECT.

18 Q. SO THE TERM "ATYPICAL CARCINOID" USED BY

19 PATHOLOGISTS IS NOT SYNONYMOUS WITH THAT TERM USED

20 IN THAT REPORT; ISN'T THAT CORRECT?

21 A. NO. THAT'S CORRECT. THAT'S CORRECT. THE

22 MAN THAT WROTE THIS REPORT, I SUSPECT HAD NO

23 KNOWLEDGE OF THE HISTOLOGY OF THE TUMOR SO HE

24 COULDN'T HAVE SAID IT IN THE PATHOLOGICAL AND I

25 BELIEVE HE IS NOT A PATHOLOGIST SO I THINK HE WAS

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1 USING IT IN THE SENSE OF THE BIOCHEMICAL.

2 MR. SIRRIDGE: WE HAVE BEEN GOING OUR

3 USUAL PERIOD OF AN HOUR AND 15 MINUTES.

4 MS. WALTERS: WE ONLY HAVE A HALF

5 HOUR LEFT.

6 MR. SIRRIDGE: LET'S TAKE A

7 FIVE-MINUTE BREAK.

8 (BRIEF RECESS)

9 BY MS. WALTERS:

10 Q. DOCTOR, IN MARCH OF 1983, MRS. CIPALLONE

11 AGAIN HAD COMPLETE BIOCHEMICAL STUDIES; IS THAT

12 CORRECT?

13 A. IN MARCH OF '83? THAT IS CORRECT, MARCH OF

14 '83.

15 Q. IS URINE I HYPHEN 3IA THE SAME AS 5-HIAA?

16 A. NO. THAT PROBABLY REPRESENTS URINARY

17 INDOLEACETIC ACID, 3-INDOLE, INDOLES, IT MIGHT BE

18 A MISTAKE IN THE ABBREVIATION BUT I WOULD GUESS IT

19 MIGHT BE URINARY INDOLEACETIC ACID. THAT'S

20 ANOTHER RELATED COMPOUND BUT THAT'S NOT

21 SPECIFICALLY ALTERED IN SEROTONIN PRODUCTION.

22 Q. WERE ALL OF THE STUDIES THAT WERE DONE IN

23 MARCH OF '83 NORMAL?

24 A. ALL OF THE STUDIES DONE IN MARCH OF '83 WERE

25 WITHIN THE NORMAL RANGE.

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1 Q. DID ROSE CIPALLONE HAVE A TUMOR IN HER BOI
2 AT THAT TIME?
3 A. I BELIEVE SHE DID HAVE TUMOR IN HER BODY
4 BECAUSE IT'S LIKELY SHE HAD TUMOR IN HER BODY.
5 DON'T KNOW EXACTLY HOW MUCH SHE HAD BUT I THINK
6 SHE DID HAVE SOME IN HER BODY.
7 Q. WHY IS IT LIKELY THAT SHE HAD IT?
8 A. WELL, BECAUSE FIVE MONTHS LATER IN THE 18TH
9 OF AUGUST, 1983, SHE HAS ABDOMINAL PAIN AND WAS
10 FOUND TO HAVE A LARGE RIGHT ADRENAL MASS THAT WAS
11 SUBSEQUENTLY DEMONSTRATED TO CONTAIN TUMOR.
12 HOWEVER, I DON'T KNOW HOW MUCH TUMOR SHE HAD
13 BECAUSE THREE MONTHS BEFORE IN DECEMBER '82, SHE
14 HAD HAD A NUMBER OF IMAGINING STUDIES, INCLUDING
15 AN ABDOMINAL CT WHICH WAS CALLED WITHIN NORMAL
16 LIMITS. SO THREE MONTHS BEFORE THIS MASS WASN'T
17 SEEN AT ALL AND FIVE MONTHS AFTER IT WAS A LARGE
18 MASS. SO I DON'T KNOW, BUT I SUSPECT SHE HAD SOME
19 TUMOR PRESENT AT THAT TIME, BUT I CAN'T SAY HOW
20 MUCH.
21 Q. WAS IT RAPIDLY GROWING?
22 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
23 THE WITNESS: I DON'T KNOW IF IT WAS
24 RAPIDLY GROWING AT THAT TIME. I HAVE NO WAY OF
25 KNOWING THAT. IT OBVIOUSLY GREW BY AUGUST OF '83

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1 BUT I HAVE NO WAY OF KNOWING THAT IT DIDN'T START
2 GROWING IN JUNE OR JULY RAPIDLY.
3 BY MS. WALTERS:
4 Q. IN AUGUST OF 1983, SHE HAD FURTHER CHEMICAL
5 STUDIES; IS THAT CORRECT?
6 A. THAT IS CORRECT.
7 Q. AND THAT INCLUDED A URINE 5-HIAA?
8 A. AUGUST OF '83? THAT INCLUDED A URINE
9 5-HIAA.
10 Q. AND THAT WAS NORMAL?
11 MR. SIRRIDGE: HOLD ON A SECOND, WILL
12 YOU, PLEASE? IT'S DIFFICULT FOR YOU TO REFER TO
13 RECORDS AND NOT PRODUCE THEM TO LOOK AT THEM.
14 MS. WALTERS: HE HAS HIS NOTES THERE
15 AND I'M NOT REFERRING TO RECORDS. I'M REFERRING
16 TO MY OWN NOTES.
17 MR. SIRRIDGE: YOU'RE REFERRING TO
18 MEDICAL RECORDS SO LET'S SLOW DOWN ENOUGH SO WE'RE
19 NOT RACING THROUGH IT.
20 THE WITNESS: YES, I HAVE THE ACTUAL
21 LAB SLIP IN FRONT OF ME NOW FROM THE 17TH OF
22 AUGUST, 1983. AND THE 5-HIAA THIS TIME IS FROM A
23 DIFFERENT LABORATORY, THE ROCHE MEDICAL
24 LABORATORY, AND THE VALUE WAS WITHIN THE NORMAL
25 RANGE.

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1 BY MS. WALTERS:

2 Q. IS THAT CONSISTENT WITH A SMALL CELL CANCER?

3 A. WELL, IT'S CONSISTENT WITH A SMALL CELL

4 CANCER AND IT'S ALSO CONSISTENT WITH AN ATYPICAL

5 BRONCHIAL CARCINOID TUMOR.

6 Q. WHEN YOU SAY "ATYPICAL BRONCHIAL CARCINOID

7 TUMOR", ARE YOU REFERRING HISTOLOGICALLY OR

8 BIOCHEMICALLY?

9 A. ACTUALLY, I'M REFERRING TO BIOCHEMICALLY.

10 Q. IS IT MORE CONSISTENT WITH A SMALL CELL

11 CANCER OR A CARCINOID OF THE BRONCHUS?

12 A. WELL, FROM THE CLINICAL COURSE --

13 Q. NOT FROM THE CLINICAL COURSE, JUST BASED ON

14 THE READING.

15 A. THE READING?

16 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.

17 OBJECT TO THE FORM OF THE QUESTION.

18 BY MS. WALTERS:

19 Q. I'M SORRY. GO AHEAD.

20 A. I CAN'T JUST GO ON THE READING BECAUSE IT

21 CAN BE COMPATIBLE TO A PERFECTLY HEALTHY

22 INDIVIDUAL JUST SEEING THE NUMBER ON THE SLIP.

23 Q. GO AHEAD BASED ON THE CLINICAL COURSE THEN.

24 A. BASED ON THE CLINICAL COURSE, IT'S

25 COMPATIBLE WITH BOTH THE SMALL CELL AND A

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1 BIOCHEMICALLY ATYPICAL CARCINOID, BUT THE
2 PREPONDERANCE OF EVIDENCE FROM THE COURSE MAKES ME
3 FEEL THAT IT'S MUCH MORE LIKELY TO BE A
4 BIOCHEMICALLY ATYPICAL CARCINOID.
5 Q. WHY IS THAT?
6 A. WELL, BECAUSE AT THE TIME THAT THIS URINE
7 WAS COLLECTED FOR THIS 5-HIAA, MRS. CIPALLONE WAS
8 RECEIVING A THOUSAND MILLIGRAMS PER DAY OF ALPHA
9 METHYL DOPA, ALDOMET, FOR HYPERTENSION, AND
10 ALDOMET HAS THE EFFECT OF INHIBITING THE ENZYME
11 DOPA DECARBOXYLASE WHICH WOULD PREVENT THE
12 PERIPHERAL TISSUES FROM CONVERTING
13 5-HYDROXYTRYPTOPHAN TO SEROTONIN AND, THUS, THERE
14 WOULD BE NO SEROTONIN TO BE CONVERTED TO
15 5-HYDROXYINDOLEACETIC ACID, 5-HIAA.
16 Q. BUT YOU HAVE NO WAY OF KNOWING WHETHER, IN
17 FACT, THAT IS THE CASE; IS THAT CORRECT?
18 MR. SIRRIDGE: WHAT IS?
19 BY MS. WALTERS:
20 Q. WHETHER THE DRUG THAT SHE WAS TAKING WAS
21 INHIBITING OTHERWISE PRESENT CHEMICAL COMPONENTS.
22 A. WELL, I THINK I DO HAVE REASON TO THINK THAT
23 BECAUSE THERE'S REPORTS IN THE LITERATURE THAT THE
24 DRUG WILL INHIBIT THE AROMATIC AMINO-ACID
25 DECARBOXYLASE. MY OWN EXPERIENCE WITH PATIENTS

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1 THAT I'VE GIVEN IT TO THEM, I KNOW IT CAN INHIBIT
2 IT. AND IN REVIEWING HER MEDICAL RECORD, SHE WAS
3 RECEIVING THERAPY WITH THAT DRUG. SO I THINK I
4 HAVE A REASONABLE EXPECTATION THAT IT COULD BE
5 RESPONSIBLE FOR INHIBITING THE DOPA DECARBOXYLASE
6 AND RESULTING IN A LOW VALUE. THAT WOULD BE
7 CERTAINLY ONE POSSIBILITY.
8 Q. WOULD THAT DRUG AFFECT OTHER READINGS OTHER
9 THAN THE 5-HIAA READING?
10 A. IT PROBABLY WOULD NOT AFFECT OTHER
11 READINGS. IF ONE HAD MEASURED
12 5-HYDROXYTRYPTOPHAN, THAT WOULD PROBABLY -- IF IT
13 WAS ELEVATED, WOULD STILL BE ELEVATED.
14 Q. AND THAT WAS MEASURED IN MARCH OF '83 AND
15 WAS NORMAL; IS THAT CORRECT?
16 A. WELL, LET ME REVIEW THAT. I DON'T THINK IT
17 WAS MEASURED. NOT IN THE URINE. MAYBE IN THE
18 BLOOD BUT NOT IN THE URINE.
19 Q. IN THE BLOOD. WOULD THAT AFFECT THE BLOOD
20 READING?
21 A. I HAVE VERY LITTLE EXPERIENCE WITH THE
22 MEASUREMENT OF 5-HYDROXYTRYPTOPHAN IN THE BLOOD.
23 I HAVE VERY LITTLE EXPERIENCE WITH THE VALUE OF
24 THAT. I'VE NEVER DONE THAT IN MY OWN LABORATORY,
25 USED THE BLOOD MEASUREMENT. SO I DON'T KNOW.

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1 AND, OF COURSE, THE OTHER QUESTION IS THAT BACK
2 THERE IN MARCH, WE REALLY DON'T KNOW HOW MUCH
3 TUMOR SHE ACTUALLY HAD IN HER BODY BECAUSE AT THAT
4 TIME THREE MONTHS BEFORE THE CT HAD BEEN NORMAL
5 AND IT WAS ONLY FIVE MONTHS LATER THAT A LARGE
6 AMOUNT OF TUMOR WAS DISCOVERED.
7 Q. DOCTOR, ARE SMALL CELL CANCER AND SMALL CELL
8 CANCER OF THE LUNG AND BRONCHIAL CARCINOIDS
9 RELATED TUMORS?
10 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
11 THE WITNESS: HOW DO YOU MEAN
12 "RELATED"?
13 BY MS. WALTERS:
14 Q. ARE THEY RELATED IN ANY SENSE?
15 A. WELL, SOME PEOPLE HAVE THE THEORY THAT THEY
16 BEAR A RELATIONSHIP TO EACH OTHER THAT THEY MAY
17 COME -- THIS IS AGAIN A THEORY -- FROM A CELL AND
18 THAT THE SMALL CELL CARCINOMA IS A VERY
19 UNDIFFERENTIATED TUMOR AND THAT THE BRONCHIAL
20 CARCINOID IS A MUCH BETTER DIFFERENTIATED TUMOR,
21 BUT THAT'S ONLY A THEORY THAT THEY ARE RELATED.
22 Q. IS THAT A THEORY THAT YOU SUBSCRIBE TO?
23 A. I SUBSCRIBE TO THE THEORY AS FAR AS IT HELPS
24 ME ORGANIZE SOME OF MY THOUGHTS ABOUT CARCINOID
25 TUMORS, BUT I DON'T KNOW -- I USE IT TO ORGANIZE

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1 MY THOUGHTS, BUT I DON'T KNOW IF THE THEORY IS, IN
2 FACT, TRUE, IF IT'S FACTUAL. IT SEEMS TO BE A
3 CONCEPTUAL THING THAT HELPS ONE ORGANIZE SOME OF
4 ONE'S NOTIONS ABOUT THE TWO, BUT THERE ARE
5 CERTAINLY SOME SIGNIFICANT DIFFERENCES IN THE
6 BRONCHIAL CARCINOIDS AND THE SMALL CELL CARCINOMAS
7 THAT MAKE ME QUESTION HOW THEY'RE RELATED.
8 Q. PART OF THIS THEORY IS THAT THERE'S A
9 SPECTRUM OR A GRADATION FROM THE BENIGN BRONCHIAL
10 CARCINOIDS TO THE MALIGNANT OAT CELL CARCINOMAS;
11 IS THAT CORRECT?
12 A. THE THEORY STATES THAT, YES. THAT'S THE
13 THEORY PROPOSED BY DR. BENCH, BENCH.
14 Q. IN 1968?
15 A. THAT'S CORRECT.
16 Q. AND IN THE MIDDLE, THERE ARE TUMORS THAT
17 TEND TO PROGRESSIVELY BECOME MORE MALIGNANT,
18 CARCINOID TUMORS THAT PROGRESS UP THE SPECTRUM
19 TOWARDS MALIGNANCY; IS THAT CORRECT?
20 A. THAT IS -- THE THEORY STATES THAT, YES.
21 Q. FROM A BIOCHEMICAL STANDPOINT, DO YOU HAVE
22 ANY NAME FOR THOSE INTERMEDIATE TUMORS?
23 A. NO, I GUESS THAT I WOULD USE THE -- I WOULD
24 ACCEPT, AS LONG AS I KNOW WHAT I'M TALKING ABOUT,
25 I WOULD ACCEPT THE DESCRIPTION, THE HISTOLOGICAL

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1 DESCRIPTION OF THE PATHOLOGISTS OF CALLING THEM
2 ATYPICAL CARCINOID TUMORS THAT SEEM TO BE -- SEEM
3 TO HAVE A GREATER MALIGNANT PROPENSITY.
4 Q. HAVE ANY BIOCHEMICAL STUDIES BEEN DONE THAT
5 DISTINGUISH BETWEEN THE HISTOLOGICALLY ATYPICAL
6 CARCINOIDS AND THE HISTOLOGICAL CLASSICAL
7 CARCINOIDS?
8 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
9 THE WITNESS: ANY STUDIES --
10 BY MS. WALTERS:
11 Q. BIOCHEMICAL STUDIES.
12 A. I'M NOT AWARE OF ANY. I'M NOT AWARE OF ANY.
13 Q. DOCTOR, WHAT IS ARGENTAFFIN STAINING,
14 A-R-G-E-N-T-A-F-F-I-N?
15 A. ARGENTAFFIN STAINING IS A TECHNIQUE -- I'M
16 DESCRIBING THIS AS A NON-EXPERT AND
17 NON-PATHOLOGIST, BUT ARGENTAFFIN STAINING IS A
18 STAINING TECHNIQUE USED BY PATHOLOGISTS TO SEE IF
19 A TUMOR STAINS WITH SILVER SALTS.
20 Q. AND WHAT IS ARGYROPHIL STAINING?
21 A. ARGYROPHIL STAINING ARE STAINS WHERE ONE
22 ALSO SEES IF THE TUMOR STAINS WITH THE SILVER
23 SALTS, BUT WHAT ONE DOES THERE IS ONE ADDS -- HAS
24 TO ADD A REDUCING AGENT TO REDUCE THE SILVER. SO
25 WHAT YOU HAVE IS THE SILVER PLUS THE TUMOR PLUS

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1 THE REDUCING AGENT. AND THE CONCEPT IS THAT
2 CERTAIN TUMORS WILL THEN STAIN WITH THE SILVER
3 STAIN IN THE PRESENCE, ONLY IN THE PRESENCE OF A
4 REDUCING AGENT, AND A REDUCING AGENT VARIES WITH
5 THE STAINS. AND I ACTUALLY COULDN'T GIVE YOU THE
6 NAMES OF ALL THE REDUCING AGENTS. THEY ARE USED
7 IN DIFFERENT MODIFICATIONS THAN THEY ARE
8 ARGYROPHIL STAINS. THEY HAVE NAMES.
9 Q. HAVE YOU EVER EXAMINED ARGENTAFFIN OR
10 ARGYROPHIL STAINING OR DISCUSSED IT IN ANY OF YOUR
11 RESEARCH PAPERS?
12 A. I HAVE DISCUSSED IT IN SOME OF MY RESEARCH
13 PAPERS. I HAVE DISCUSSED IT USUALLY IN THE
14 INTRODUCTION OR THE DISCUSSION SECTION.
15 SPECIFICALLY IN MY OWN RESEARCH, I HAVEN'T
16 ACTUALLY DONE IT AS PART OF MY RESEARCH.
17 Q. DOES SEROTONIN HAVE ANYTHING TO DO WITH
18 ARGENTAFFIN AND ARGYROPHIL STAINING?
19 A. SEROTONIN SEEMS TO HAVE TO DO WITH
20 ARGENTAFFIN STAINING.
21 Q. IN WHAT WAY?
22 A. WELL, SEROTONIN IS A VERY POTENT REDUCING
23 AGENT AND IT WILL REDUCE THE SILVER SALTS TO
24 ELEMENTAL SILVER OR WHATEVER THE BIOCHEMISTRY OF
25 THE THING IS AND THEN THE TISSUES WILL STAIN WITH

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1 THE SILVER AND THE GRANULES IN THE TUMOR WILL
2 STAIN BLACK, WHICH IS THE COLOR OF THE REDUCED
3 SILVER. AND SEROTONIN IS ONE OF ONLY A HANDFUL OF
4 THINGS WHICH IS CAPABLE OF REDUCING THE SILVER
5 WITHOUT AN ADDED REDUCING AGENT.
6 Q. IS THE SEROTONIN STORED IN THE GRANULES AND
7 THAT'S WHAT CAUSES IT TO STAIN?
8 A. THE SEROTONIN IS STORED IN THE GRANULES OF
9 THE CARCINOID TUMOR. USUALLY THE MAJORITY IS IN
10 THE GRANULES.
11 Q. AND DO CARCINOID TUMORS TEND TO STAIN
12 POSITIVE?
13 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
14 THE WITNESS: WITH ARGENTAFFIN
15 STAINS, SOME CARCINOID TUMORS WILL STAIN POSITIVE
16 BUT OTHERS WILL NOT.
17 BY MS. WALTERS:
18 Q. HOW ABOUT SMALL CELL CANCERS?
19 A. I AM NOT AWARE OF ANY SMALL CELL CANCERS
20 STAINING WITH ARGENTAFFIN STAINING, BUT IT MAY
21 BE. THAT'S JUST SOMETHING I HAVE NOT READ, BUT
22 I'M NOT AWARE OF THAT.
23 Q. SO IF A TUMOR DOES NOT STAIN POSITIVE, IS
24 THAT MORE CONSISTENT WITH A SMALL CELL CANCER THAN
25 WITH A CARCINOID TUMOR?

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1 A. WELL, ARE WE TALKING ABOUT THE ARGENTAFFIN
2 OR THE ARGYROPHIL?
3 Q. ARGENTAFFIN.
4 A. NO, I DON'T THINK ONE CAN USE THAT TO
5 DISTINGUISH THE TWO, ARGENTAFFIN, BECAUSE THERE
6 ARE SOME CARCINOID TUMORS THAT DON'T STAIN WITH
7 THE ARGENTAFFIN STAINS THAT ARE, IN FACT,
8 CARCINOID TUMORS. CARCINOID TUMORS OF THE ILEUM
9 AND SO FORTH THAT DON'T HAPPEN TO CONTAIN
10 SEROTONIN WILL NOT STAIN WITH THE SILVER STAIN.
11 Q. I'M TALKING ABOUT OF THE LUNG.
12 A. CARCINOID TUMORS OF THE LUNG THAT DON'T
13 CONTAIN SEROTONIN WON'T STAIN WITH THE ARGENTAFFIN
14 BUT, YET, THEY ARE CARCINOID TUMORS BY OTHER
15 CRITERIA, HISTOLOGICAL AND BIOCHEMICAL AND
16 ULTRA-STRUCTURAL AND SO FORTH.
17 Q. SO SMALL CELL CANCERS THAT DON'T CONTAIN
18 SEROTONIN WOULD ALSO NOT STAIN; IS THAT CORRECT?
19 (OBJECTION) MR. SIRRIDGE: OBJECT TO THE FORM.
20 THE WITNESS: COULD YOU SAY IT ONE
21 MORE TIME?
22 BY MS. WALTERS:
23 Q. SMALL CELL CANCERS THAT DO NOT CONTAIN
24 SEROTONIN WOULD ALSO FAIL TO STAIN?
25 (OBJECTION) MR. SIRRIDGE: STILL OBJECT TO THE

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1 FORM.

2 THE WITNESS: OF COURSE, I'M NOT AN

3 EXPERT AND I'M NOT AWARE OF ANY SMALL CELL

4 CARCINOMA TUMORS STAINING. I'M NOT AWARE OF THEM

5 STAINING SO I CAN'T SAY THAT THEY DON'T STAIN IF

6 THEY DON'T HAVE THE SEROTONIN OR DO HAVE IT. I'M

7 NOT AWARE OF THEM STAINING OF THE ARGENTAFFIN

8 STAIN.

9 BY MS. WALTERS:

10 Q. DOCTOR, HAVE YOU EVER SMOKED?

11 A. I SMOKED FOR A BRIEF TIME WHEN I WAS IN MY

12 YOUNGER YEARS, PROBABLY IN MY LAST YEAR OF HIGH

13 SCHOOL INTERMITTENTLY AND PERHAPS IN THE EARLY

14 PART, OF MY RECOLLECTION, IS THAT I SMOKED.

15 Q. HOW MUCH DID YOU SMOKE?

16 A. MY RECOLLECTION IS I NEVER SMOKED MORE THAN

17 HALF A PACK OF CIGARETTES AND I WOULD ESTIMATE I

18 PROBABLY DID IT FOR HALF A YEAR ON AND OFF.

19 Q. DO ANY MEMBERS OF YOUR FAMILY SMOKE?

20 A. WHAT FAMILY, YOU MEAN IMMEDIATE FAMILY?

21 Q. IMMEDIATE FAMILY, CHILDREN, WIFE.

22 A. MY WIFE DOESN'T SMOKE. I HAVE THREE

23 CHILDREN, A 14-YEAR-OLD SON WHO DOESN'T SMOKE, A

24 22-YEAR-OLD DAUGHTER WHO DOESN'T SMOKE AND A

25 21-YEAR-OLD DAUGHTER WHO IS IN COLLEGE WHO MAY

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1 SMOKE. I'M NOT CERTAIN IF SHE DOES.

2 Q. HAVE YOU EVER SPOKEN TO HER ABOUT SMOKING?

3 (OBJECTION) MR. SIRRIDGE: I'M GOING TO OBJECT AT

4 THIS POINT.

5 MS. WALTERS: THESE SAME QUESTIONS

6 WERE ASKED OF DR. COHEN YESTERDAY AT HIS DEP SO I

7 WAS TOLD TO COVER THIS AREA.

8 THE WITNESS: HAVE I EVER TALKED TO

9 HER? I THINK ON OCCASION I TOLD HER I WOULD BE

10 HAPPIER SHE DIDN'T SMOKE WHEN I THOUGHT SHE WAS

11 SMOKING.

12 BY MS. WALTERS:

13 Q. WHY IS THAT?

14 A. BECAUSE I HAVE THE IMPRESSION, THE GENERAL

15 IMPRESSION, THAT SMOKING IS NOT GOOD FOR ONE'S

16 HEALTH.

17 Q. IN WHAT WAY?

18 A. WELL, I THINK THAT SMOKING -- I STOPPED

19 SMOKING BECAUSE I REALLY DIDN'T ENJOY IT WHEN I

20 WAS IN COLLEGE AS A STUDENT. I THINK THAT IT'S

21 ASSOCIATED WITH CERTAIN RISK FACTORS AS A RISK

22 FACTOR FOR CERTAIN ILLNESSES. IF ONE SMOKES FOR A

23 LONG PERIOD OF TIME AND A SUBSTANTIAL AMOUNT, IT

24 SEEMS TO BE ASSOCIATED WITH THERE'S A RISK FACTOR.

25 Q. WOULD THAT INCLUDE LUNG CANCER?

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1 A. IT SEEMS TO BE A RISK FACTOR FOR CERTAIN
2 FORMS OF LUNG CANCER, AT LEAST THAT'S MY KNOWLEDGE
3 OF IT, AND ALSO PERHAPS FOR CORONARY ARTERY
4 DISEASE AND EMPHYSEMA, IT SEEMS TO BE A RISK
5 FACTOR.
6 Q. DOCTOR, YOU SENT SOME THINGS TO MR. SIRRIDGE
7 BY LETTER OF DECEMBER 1, 1986. ONE OF THEM IS AN
8 FDA DRUG BULLETIN REGARDING CEA.
9 MR. SIRRIDGE: WE'RE AFTER 5:30.
10 MS. WALTERS: I JUST HAVE A COUPLE OF
11 QUESTIONS.
12 MR. SIRRIDGE: JUST BECAUSE YOU WANT
13 TO RUSH THROUGH DOESN'T MEAN WE'RE GOING TO RUSH
14 THROUGH AND NOT FIND WHAT YOU'RE TALKING ABOUT.
15 THE WITNESS: I SENT HIM A DRUG --
16 BY MS. WALTERS:
17 Q. WHY DID YOU SEND THAT TO MR. SIRRIDGE?
18 A. THAT PARTICULAR THING I SENT TO MR. SIRRIDGE
19 BECAUSE WE HAD HAD A MEETING, MR. SIRRIDGE AND I
20 HAD HAD A MEETING, FIRST MEETING WE ACTUALLY HAD
21 CONCERNING THIS CASE, THIS MEDICAL PROBLEM. AND I
22 HAD TOLD MR. SIRRIDGE, I BELIEVE, AT THE MEETING
23 WHEN I REVIEWED THE CHART THAT I NOTICED THAT MRS.
24 CIPALLONE HAD A NORMAL TITER OF CEA,
25 CARCINOEMBRYONIC ANTIGEN. IT'S AN ANTIGEN THAT'S

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1 MEASURED IN THE BLOOD. AND MRS. CIPALLONE HAD HAD
2 A NORMAL VALUE OF THAT. AND I HAD TOLD MR.
3 SIRRIDGE THAT, ALTHOUGH AT THE MEETING I DIDN'T
4 HAVE THE PAPER, I RECALL HAVING DONE A STUDY SOME
5 YEARS BEFORE IN PATIENTS WITH CARCINOID TUMORS AND
6 FOUND THAT, IN GENERAL, THE PATIENTS WITH
7 CARCINOID TUMORS TEND TO HAVE A NORMAL LEVEL OF
8 THIS ANTIGEN OR A LEVEL THAT WOULD NOT BE AS HIGH
9 AS ONE MAY ANTICIPATE IF THEY HAD HAD ANOTHER TYPE
10 OF TUMOR SUCH AS A COLON TUMOR OR SOMETHING. SO I
11 SENT MR. SIRRIDGE THIS REPORT, WHICH REALLY THE
12 PART I CIRCLED ON THE REPORT WAS THE PATIENTS WITH
13 LUNG TUMORS, LUNG CANCERS, PULMONARY CARCINOMAS,
14 HAD A FAIRLY HIGH INCIDENCE OF ELEVATED CEA
15 ANTIGEN.
16 Q. DO YOU KNOW WHETHER PATIENTS WITH SMALL CELL
17 LUNG CANCER HAVE ELEVATED LEVELS OF CEA?
18 A. THIS REPORT ACTUALLY DID NOT BREAK IT DOWN
19 INTO CELL TYPES AND I DON'T HAVE ANY SPECIFIC
20 KNOWLEDGE ABOUT THE SMALL CELL PATIENTS. IT
21 WASN'T CONTAINED IN THIS REPORT.
22 Q. IS THIS BULLETIN THE ONLY INFORMATION THAT
23 YOU HAVE ABOUT CEA ANTIGENS IN LUNG CANCER
24 PATIENTS OTHER THAN CARCINOIDS?
25 A. I PROBABLY HAVE OTHER MATERIAL THAT I USED,

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1 FOR INSTANCE, WHEN I WROTE THIS REPORT ON CEA
2 ANTIGEN WITH THE PATIENT WITH CARCINOID TUMORS. I
3 PROBABLY HAVE OTHER MATERIALS, OF COURSE, SOMEWHAT
4 OLDER BECAUSE I WROTE THE REPORT IN 1975 AND I
5 REALLY HAVEN'T REVIEWED TO FIND THAT MATERIAL AND
6 SEE IF I DID HAVE OTHER INFORMATION.
7 Q. AS YOU SIT HERE TODAY, YOU DON'T KNOW
8 WHETHER PATIENTS WITH SMALL CELL CANCER HAVE
9 ELEVATED LEVELS OF CEA; IS THAT CORRECT?
10 A. I DON'T SPECIFICALLY KNOW THAT. I DON'T
11 SPECIFICALLY KNOW THAT, ALTHOUGH I WOULD ASSUME IN
12 THIS LIST OF PEOPLE WITH PULMONARY CARCINOMA THERE
13 MUST HAVE BEEN A SUBSTANTIAL NUMBER THAT HAD SMALL
14 CELL. MOST COMPILATIONS OF PEOPLE WITH LUNG
15 CANCER, THEY USUALLY INCLUDE A GOOD PERCENTAGE
16 WITH SMALL CELL. AND I JUST SIMPLY SENT THAT FOR
17 MR. SIRRIDGE'S INTEREST POINTING OUT THAT I HAD
18 MAINLY DONE THAT, OF COURSE, IN PATIENTS WITH
19 CARCINOID TUMORS OF GASTROINTESTINAL ORIGIN.
20 MR. SIRRIDGE: NOTE FOR THE RECORD I
21 HAVE LOTS OF INTEREST IN THIS CASE. WE'RE AT
22 5:35.
23 MS. WALTERS: I HAVE TO ASK HIM A
24 QUESTION ABOUT ITEM SIX SINCE YOU ONLY PROVIDED
25 ONE PAGE OF THE ITEM.

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1 BY MS. WALTERS:

2 Q. DOCTOR, WHAT JOURNAL IS THAT ARTICLE FROM?

3 A. THAT IS, I THINK, ALL I PROVIDED TO MR.

4 SIRRIDGE, WASN'T IT? I JUST SENT YOU THE TABLE?

5 MR. SIRRIDGE: YES.

6 THE WITNESS: DID I IDENTIFY WHAT THE

7 JOURNAL WAS? I DIDN'T WANT TO SPEND TOO MUCH

8 MONEY XEROXING. THAT WAS ALL I SENT HIM, I

9 BELIEVE. AM I RIGHT, MR. SIRRIDGE? I CAN'T ASK

10 THAT.

11 BY MS. WALTERS:

12 Q. WHAT JOURNAL IS THAT FROM?

13 A. WHAT JOURNAL IS THAT FROM? I CANNOT

14 HONESTLY REMEMBER WHAT JOURNAL IT'S FROM. IT'S

15 POSSIBLE IT WAS A TEXTBOOK OF CANCER MEDICINE.

16 Q. DO YOU HAVE THAT INFORMATION AT HOME?

17 A. I MAY HAVE THAT INFORMATION AT HOME. I

18 COULD LOOK FOR IT.

19 Q. (REQUEST) AS A THIRD REQUEST, COULD YOU

20 LOCATE THAT AND GIVE THAT INFORMATION TO MR.

21 SIRRIDGE FOR ME?

22 A. I WILL.

23 MR. SIRRIDGE: I'LL NOTE THE

24 REQUEST.

25 MS. WALTERS: THANK YOU, MR.

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1 SIRRIDGE. I GUESS THAT'S ALL WE HAVE TIME FOR.

2 (WITNESS EXCUSED)

3

4

5 Jerome M. Feldman M.D.

6

7 JEROME M. FELDMAN, M.D.

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1 C E R T I F I C A T E

2 I, GEORGANNE FARES, A NOTARY PUBLIC AND
3 CERTIFIED SHORTHAND REPORTER OF THE STATE OF NEW
4 JERSEY AND A COMMISSIONER OF DEEDS OF THE STATE OF
5 PENNSYLVANIA, DO HEREBY CERTIFY THAT PRIOR TO
6 THE COMMENCEMENT OF THE EXAMINATION,
7 JERMONE M. FELDMAN, M.D.
8 WAS DULY SWORN BY ME TO TESTIFY TO THE TRUTH,
9 THE WHOLE TRUTH AND NOTHING BUT THE TRUTH.
10 I DO FURTHER CERTIFY THAT THE FOREGOING IS
11 A TRUE AND ACCURATE TRANSCRIPT OF THE TESTIMONY
12 AS TAKEN STENOGRAPHICALLY BY AND BEFORE ME AT THE
13 TIME, PLACE AND ON THE DATE HEREINBEFORE SET
14 FORTH.
15 I DO FURTHER CERTIFY THAT I AM NEITHER A
16 RELATIVE NOR EMPLOYEE NOR ATTORNEY NOR COUNSEL OF
17 ANY OF THE PARTIES TO THIS ACTION, AND THAT I AM
18 NEITHER A RELATIVE NOR EMPLOYEE OF SUCH ATTORNEY
19 OR COUNSEL AND THAT I AM NOT FINANCIALLY
20 INTERESTED IN THIS ACTION.
21
22 Georganne Fares
GEORGANNE FARES, C.S.R.
23 NOTARY PUBLIC, STATE OF NEW JERSEY
MY COMMISSION EXPIRES MARCH 30, 1991
24 CERTIFICATE NO. 1144
DATE: SEPTEMBER 3, 1987
25

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